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### **PROGRESS REPORT**



# UNPUBLISHED PRELIMINARY DATA

A Technique for Testing Heart Function by Analysis of its Vibration Spectrum

Reference:

National Aeronautics and Space Administration

Research Grant N<sub>s</sub>G-289/05-12-001

Submitted by:

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#### FOREWORD

The following report was prepared by Clarence M. Agress, M.D. and Stanley Wegner of the Cardiovascular Research Laboratory, Cedars of Lebanon Institute for Medical Research, Los Angeles, California. The authors wish to express their appreciation to Shigeo Nakakura, M.D., Eugene Lehman, Ph.D. and Gerald Labins for their contributions to this report, to Dixie J. Day for her valuable assistance in manuscript composition and to Stanley Beckman for preparation of the illustrations.

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#### 1.0 GENERAL INTRODUCTION

The accomplishments during the initial period of Grant NsG-289/05-12-001 have resulted in significant advances toward the ultimate goal of assessing heart function by a simple external technique. One of the most difficult steps was to select those parameters which can detect early decompensation of the heart and to eliminate those which are merely measurements of physical fitness. To this purpose, Section I selects and clarifies from an extensive literature, those parameters which are illuminating. It was most interesting to discover that cardiac physiology has come full circle -- back to the Frank-Starling principle.

Section II presents the animal data obtained from the use of established cardiac performance measurements. Acute experiments contrast the responses to various stresses imposed on normal and myocardial damaged dogs. Other experiments measure, with implanted heart strain gauges, the effects of exercise on dogs trained to run on treadmills. Thus the directly measured volume changes of the heart could be compared to the simultaneously recorded

vibrocardiograms in intact, unanesthetized animals.

Section III compares the performance of athletes, sedentary normal subjects, "functionally normal" patients who are asymptomatic after recovery from heart attacks and coronary diseased subjects whose activities are restricted by angina. An interesting conclusion is developing as a result of this study. The data indicate that the exercise vibrocardiogram without posture change does not separate normal subjects from patients with ischemic heart disease, probably because the neurohumoral influences of exercise on the contractility of the myocardium seem to mask the disease. On the other hand, it is surmised that postural changes -- as standing to lying without exercise -- impose a stress due in part to a sudden increase in venous return with little or no change in contractility. The vibrocardiogram seems remarkably well suited for this test of function which is now being vigorously subjected to statistical analysis.

Detailed scrutiny of the vibrocardiographic wave forms has been conducted in both animals and man. Criteria have been

established for wave intervals which accurately identify
the various periods of the cardiac cycle such as isometric contraction, ejection, rapid filling, etc. The determinants of these periods are being formulated; e.g., those
which are rate dependent can be separated from those which
are not. It appears that certain states such as hypoxia can
probably be identified by the alterations of these intervals.

The measurement of ejection time alone, contrary to the literature, has failed to discriminate the stress responses of normal from abnormal subjects. The VbCg, which readily measures both the ejection and isometric contraction times, affords a function test based on the comparison of these two intervals.

The most promising development is the estimation of heart function from an evaluation of the input-output response of the ventricle; i.e., initial ventricular tension is compared to the resulting stroke work of the ventricle. It appears that this information can be obtained from the VbCg. If further investigation supports this observation, a significant tool will indeed have been developed.

1.10 Literature Survey of Ventricular Function Measurements

#### 1.11 <u>Introduction</u>

Attempts to measure the ability of the heart to perform under stress can be found as early as 3000 B.C. in the Edwin Smith Surgical Papyrus of the Egyptians. But it was not until Galileo, who related the rate of the pulse to the rate of a pendulum swinging, that any precision of measurement was introduced. Half a millenium later with the highly refined methods of research, precision instruments, computers and factor analysis of today, the ability to measure the function of the heart is still limited.

Measurements designed to test physical fitness (performance) and the influence of training must be separated from those designed to show cardiac decompensation (function). It is much less difficult to describe changes in performance than it is to detect decompensation or to discriminate between normal and abnormal function. The extensive literature on cardiac muscle physiology is largely devoted to studies describing the determinants of performance. (Witness the controversy over the application of the Frank-Starling

hypothesis to the intact organism.) Relatively little attention has been given by physiologists to the recognition of decompensation and then only when severe degrees of injury, such as frank failure, exists.

Our interests lie in those measurements which will discriminate at the <u>earliest</u> opportunity the inability of the cardiovascular system to meet a challenge at a time when, if recognized, such decompensation can hopefully be reversed. To this purpose, most of the important papers on heart performance, from those describing the isolated muscle strip to the intact unanesthetized human experiments, have been reviewed. Our objectives were: 1. to evaluate those general parameters which are largely tests of physical fitness; 2. to define the measurements of ventricular performance which the best investigators have found reliable, and 3. to select those measurements which can be expected to discriminate normal from abnormal function.

Some means is sorely needed to measure ventricular performance and function free of laboratory or surgical

encumbrance, adaptable for use in the office, clinic or space chamber. Therefore, those parameters found to be most dependable will be tested using practical techniques with particular attention to the analysis of precordial vibrations.

#### 1.12 Heart Rate

Even before Aristotle, it was known that heart rate has some relationship to physical fitness and that the pulse rate of an athlete will be slower for a given work-load than that of a healthy, untrained subject. Controlled (1) studies were described at least as early as 1904

In general it may be said that for a specific work load, the better the physical condition of the subject, the smaller the increase in heart rate (HR) and the more rapid the return to the resting level. However, HR changes can be induced by physiological factors such as age, sex, ingestion of food, fatigue, autonomic control; by environmental influences such as temperature, oxygen tension, and barometric pressure; by training; and by all the variants imposed by disease. Such wide influences make HR

While HR responses to stress are helpful in evaluating physical fitness, the overlap is too great to establish useful criteria for the estimation of ventricular function.

### 1.13 <u>Heart Rate Blood Pressure Product</u>

The work of Katz has shown that the HR x BP product is more linearly related to oxygen consumption  $(qO_2)$  than is cardiac output; that is,  $\frac{qO_2}{HR \cdot BP} = K$ . Stroke  $qO_2$  is then linearly dependent on BP. These relationships hold for a wide range of HR and BP changes but unfortunately they do not hold for marked hypoxia, increased catecholamines, digitalis administration, etc. Furthermore, the  $qO_2$  may be augmented when muscle shortening is increased (Fenn effect) and when velocity of shortening is increased. Thus this HR·BP product is useful, since it reflects the rate of oxygen consumption, but it furnishes only a rough index of ventricular function.

#### 1.14 Respiratory Measurements

The determinations of vital capacity, breath-holding time, maximal breathing capacity and maximal expiratory force have been shown to be worthless as functional tests on

(10) healthy subjects

1.15 Stroke Volume

(11) (12)

in 1895, and Patterson, Piper and Starling Frank 1914, formulated the concept that "The increased energy of the heart's contraction under conditions of increased pressure and increased inflow must be ascribed to alterations in the length of the muscle fibers at the beginning of and during their state of excitation and not to changes in the tension on the fibers". The inconsistent relation of ventricular diastolic pressure and ventricular diastolic volume and the difficulties of measuring ventricular volume (fiber length), delayed the proof for the extension of this laboratory observation to the intact human heart. Various objections to the Frank-Starling hypothesis were raised, such as Anrep's finding in Starling's own laboratory that epinephrin produced a more forceful response (13)without an increase in heart size (end-diastolic volume)

The stroke volume response of the ventricle to exercise has also been confused by the failure of many investigators to (14) appreciate the marked influence of posture. In 1934 Nylin showed that cardiac size is maximal when the normal human

subject is at rest and recumbent. When the subject stood, the heart became smaller. Exercise increased the size of the heart, but it never returned to the size of that found in recumbency. This finding also has been cited as evidence against the general applicability of the Frank-Starling principle. Rushmer using implanted strain gauges, was able to study left ventricular rather than total cardiac volume and found that exercise usually caused a decrease in both systolic and diastolic left ventricular diameters independent of changes in rate. Chapman et al , using biplane cinefluorography on the intact dog during exercise, showed a direct relationship between the end-diastolic left ventricular volume and stroke work. Although stroke work was found to increase with exercise, end-diastolic (EDV) and end systolic (ESV) left ventricular volume decreased, confirming Rushmer's observations. Sarnoff has sought to explain this phenomenon by the concept of a "family of curves" where "if the effective catecholamine stimulus remains constant, the contraction of the ventricle varies directionally with its end-diastolic pressure (EDP) and

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fiber length; if the EDP and fiber length remain constant, the contraction of the ventricle varies directionally with the effective catecholamine stimulus." Braunwald has shown that the "contractility" of the ventricle is increased in exercise (increased sympathetic discharges) by an increment in the catecholamine content of the myocardium. By these means, the ventricle can produce increased tension without a corresponding increase in fiber length. Holmgrem et al , at right heart catheterization, found that cardiac output during exercise increased linearly with the oxygen uptake. From rest to work the stroke volume (SV) increased only 8%; moreover, as the work load increased, the SV declined to the resting level. They found a high correlation between SV and the blood volume (total amount of hemoglobin) and felt that the SV was regulated to the optimal amount of blood in the vascular system, there being a (20)direct relationship when measured in recumbency

Yang Wang et al studied the effects of posture on the SV of man during exercise. A steady state was reached in

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2 minutes in most subjects, but the difficulty of achieving a steady state in the upright position during prolonged severe exercise was demonstrated, probably because the same work level is not maintained even at a constant treadmill speed. In the supine position, the stroke index averaged 54 ml.; on standing it fell to Mild exercise while standing caused a rise to 54 ml. and severe exercise to 59 ml. Thus even mild exercise causes the stroke index to increase toward the value in the supine position, to show only a small additional increase even with severe exercise. If the SV during severe upright exercise is compared to the supine resting value, the increase is only -9 to +23%. change under these conditions is +156 to +190%. SV is compared to the resting standing value, the increase with exercise is +61 to +110% compared with a (22) HR change of +77 to +122%. Reeves et al measured cardiac output at catheterization on normal subjects while supine, standing and during treadmill exercise. Total A-V oxygen difference, oxygen uptake and cardiac outputs were quite different indicating that different

circulatory mechanisms, especially in the legs, are involved in supine and standing exercise. Similar (23) results have been obtained by Bruce et al (24) Wilson measured left ventricular diameter continuously with an indwelling gauge. Maximum dimensions were obtained in the supine position with reduction when upright. With exercise there was a gradual increase in diameter. It is apparent, therefore, that change in posture alters the cardiac output response to exercise.

1.16 Cardiac Output

(25)Since 1898 when Zuntz and Hagemann first measured the cardiac output (CO) of the horse by the Fick principle (40 years before it was used in man), physiologists have been interested in calculating the volume of blood pumped by the heart. From the earliest tedious gasometric techniques to modern cardiac catheterization and dye dilution calculators, the measurement of the product of SV and HR, adjusted for body surface area (cardiac index) has been regarded as a valuable indicator of the (26)heart's ability to respond to stress. Since Lindhard in 1915, first measured it in man, the CO response to exercise has been used to assess heart function. His observation that oxygen consumption during exercise increased in linear fashion with increase in CO, has been repeatedly substantiated by many subsequent investigators.

Since McMichael introduced the concept that the response of the heart to exercise might be more important than its performance at rest, the CO response to exercise

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has been studied extensively in an attempt to relate the capacity of the diseased heart to that of the normal heart. Measurements of CO after exercise in disease states such as in mitral stenosis showed, in general, inadequate responses and, in some instances, severe impairment, but there is poor correlation with disability. Studies after mitral valvulotomy are not conclusive and so far have not helped to distinguish the parts played by mechanical and myocardial factors. In aortic stenosis and hypertension, it has been found that the left ventricle is able to eject blood against a heavy pressure load without there appearing much decrease in CO either at rest or after exercise In ischemic heart disease, large areas of ventricular muscle can be infarcted, yet the CO may be within normal range. Even when congestive heart failure is present, there is no close connection with the level of CO. Chapman and Fraser measured the CO of patients who had had myocardial infarction six months previously and found that their exercise responses were the same as found in a normal group of the same age. Furthermore, even when dyspnea and angina are present in

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ischemic heart disease, there is no close correlation (31) with the CO at rest nor the response to exercise .

It seems to be established, therefore, that HR, SV and CO determinations at rest or after exercise are valuable indicators of physical fitness but they do not give reliable estimates of cardiac function.

#### 1.17 Oxygen Consumption

In a review of the literature, Astrand found that maximal oxygen consumption (qO<sub>2</sub>) declines with age from a maximum of 50 cc/Kg/min. at 25 years to 41 cc. at 40, 39 cc. at 50 yrs, 35 cc. at 60 yrs. and 30 cc. at 70 yrs. Elite athletes may reach 82 cc./Kg/min. The severity of the exercise can be checked by determining the blood lactic acid level. Maximal work with the arms produces less oxygen uptake than maximal work with the legs, and work with arms and legs produces greater maximal uptakes than either one alone.

The aerobic capacity is probably the best measure of a person's physical endurance. At 50% capacity, the pulse

rate averages 128; at 70%, 154. Best results for work tests are obtained at heart rates of 125 to 170. In general, the  $qO_2$  and the HR increase linearly with increase of CO. But measurement of maximum working capacity by determining the maximum  $qO_2$  is not always a reliable indication of the individual's (33) working capacity .

1.18 <u>Definition of Ventricular Performance Measurements</u>
In order to define cardiac performance, a description of the terms used in measuring the mechanical properties of cardiodynamic responses is first necessary. These terms consist of measurements of pressure and volume occurring as a function of time during the cardiac cycle. Such parameters serve to relate in measureable terms, the quantities describing the pumping action of the ventricles. They can be summarized as follows:

(See figure 1)

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rate averages 128; at 70%, 154. Best results for work tests are obtained at heart rates of 125 to 170. In general, the  $q0_2$  and the HR increase linearly with increase of CO. But measurement of maximum working capacity by determining the maximum  $q0_2$  is not always a reliable indication of the individual's (33) working capacity .

1.18 <u>Definition of Ventricular Performance Measurements</u>
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(See figure 1)

MEASURE	MENTS OF VENTE	RICULAR PERFOR	MANCE
PARAMETER	FORMULA	TERM	DESCRIPTION
PRESSURE mmHg	Force/Area  1/t <sub>2</sub> t <sub>1</sub>	End Diastolic Press  Mean Arterial Pr (1/3 PP+DP)  Pulse Pressure	MAP PP
PRESSURE TIME PRODUCTS mmHg/Sec	P x t ∫Pdt=Impulse (Fxt)	Tension Time Indices Pressure Time/beat	STATIC
PRESSURE TIME QUOTIENTS mmHg/Sec	ΔP/Δt dP/dt	Ventricular Slope 1 st Derivative Press	
VOLUME ml/beat	v	End Diastolic V End Systolic V Stroke Volume	ESV EDV RATIO EDV-ESV
VOLUME TIME QUOTIENTS L/min – ml/beat	V/t ΔV/Δt dV/dt	Cardiac Output  Mean Systolic Ejection Rate  Peak Ejection Rate	Stroke Volume Ejection Time
VOLUME PRESS PRODUCTS ml x mmHg kg M/min	∫PdV=Work SV x MAP	Stroke Work	V P
VOL PRESS TIME QUOTIENTS ml x mmHg Sec	dW/dt SV × MAP Ejection Time	Stroke Po <del>we</del> r	Stroke Work Ejection Time

Figure 1

TIME

Sec

A. Isovolumic Contr

C. Isovolumic Relax
D. Diastolic Periods

B. Ejection

1. Pressure:

Pressure defines the force exerted by the myocardium on a unit area of blood. It is related to tension in the heart by the law of Laplace (tension = pressure x radius for a cylinder). This measurement is used as an instantaneous value (i.e. EDP, peak systolic pressure) or as a mean value (mean arterial pressure).

#### 2. Pressure - Time Products

The pressure time product represents the accumulated force exerted by the ventricle on the blood during a measured period of time and is analagous to the term impulse (34) ( I = \int Fdt). Wiggers was the first to recognize the importance of this measurement and termed it the "tension time index". His measurements included areas under the ventricular pressure curve in the regions of isometric contraction,

ejection above aortic diastolic pressure

(kinetic), ejection below aortic diastolic

pressure (static), and isometric relaxation.

(35)

Later, Sarnoff adapted the kinetic

(36)

ejection area, and Gorlin using the

same parameter, named it the pressure time

per beat.

A further measurement of ventricular impulse (37)
has been described by Rushmer who considered that the summed force acting on the blood during the initial phase of ejection was a significant property. This measurement involves the integration with respect to time of the blood acceleration curve (obtained by means of a flowmeter) from the onset of ejection to peak ejection and is called the initial ventricular impulse.

The comparison of this measurement to other impulse measurements has not been accomplished, but Rushmer expressed the opinion that

measurement of precordial movements might well reflect this value.

#### 3. Pressure-time quotients

The importance of pressure time quotients or rates of pressure change was first noted by (38)Frank who found that the slope of the ventricular pressure curve was increased as a result of greater initial ventricular tension. He used this finding to express a greater ventricular "force". Wiggers also observed that the slope of the ventricular pressure curve could be used as a measure of its performance. More recently, these measurements have been revived in the (40,41)form of ventricular pressure derivatives which present the instantaneous rates of pressure change (dP/dt) rather than the average rate of change as was used by Starling and Wiggers. The significance of these measurements lies in their ability to define the

rate of development of force throughout the cardiac cycle.

#### 4. Volume

Volume defines the quantity of blood within the cardiac chambers and is measured at discrete intervals during the cardiac cycle. These are: the volume at the termination of diastole (EDV), the volume at the termination of systole (ESV) the difference between these two volumes (SV) and, more recently, the ratio of ESV to EDV ( $\frac{ESV}{EDV}$ ).

#### 5. Volume-time Quotient

The volume time quotient represents the cardiac output and the significance of this property has been well established. Other volume time quotients describe the rate of ventricular ejection (MSER). Average values of this function are obtained by dividing stroke volume by ejection time, but true values can only be obtained by the use of flowmeters. These

measurements correspond to the rate of ventricular fiber shortening for a given end-diastolic volume.

#### 6. Volume Pressure Products

The volume pressure product describes the external work performed by the ventricle with the exception of the kinetic energy imparted to the blood. The latter has been shown to be a small factor — around 2% of the total energy and, therefore, can be neglected. This measurement, in the strict sense, can only be obtained from the area within the ventricular pressure volume loop ( $SW = \int P dv$ ). Generally, the mean values of pressure and stroke wolume are multiplied to provide this measurement which is termed stroke work.

#### 7. Volume Pressure Product/time

The measurement of the rate of the volume pressure product change describes the power

generated by the heart. The measurement is obtained by differentiating the stroke work with respect to time. An average value of stroke power is obtained by dividing stroke work by ejection time.

#### 8. Time

The duration of cardiac events has recently received greater attention. Measurements have been made on all phases of the cardiac cycle but those dealing with isometric contraction and ejection have shown the most promise. (See Section on Isometric Contraction and Ejection Time.)

## 1.19 <u>Use of These Parameters in Estimation of</u> <u>Heart Performance</u>

Pressure is the easiest property to measure and its use as a function measurement has been well established. Studies with pressure time integrals and derivatives are more (34) recent. Wiggers was the first to consider that the ratio of the Kinetic to Static ejection tension time

index (see figure 1) provided a means of measuring cardiac "efficiency". This ratio as such has not been used, but the kinetic tension time index (TTI) was adopted by both Sarnoff and Katz of these investigators showed that the TTI was (9) directly related to myocardial oxygen uptake. Katz found, however, that this relationship was true only in the absence of hypoxia, alterations in circulating catecholamines, etc. Levine and Wagman applied the TTI in normal subjects and patients with congestive failure. They found that the resting values were nearly the same. After exercise the TTI increased in normals and remained unchanged in subjects in failure, but clear separation of the two groups could not be achieved. Considering the severity of the dysfunction in the failure group, the sensitivity of this index can be questioned; furthermore, studies in animals under

Derivatives of intraventricular pressure are currently being employed as standard measurements of myocardial (39) performance. Wiggers noted that "when myocardial

induced pathologic states have yet to be reported.

ischemia was induced, the slope of the left ventricular pressure curve decreased in the face of rising end-diastolic pressure". Reeves et al performed an extensive study on the derivative of left ventricular pressure under a variety of hemodynamic states. They concluded that the maximum value of the first derivative of left ventricular pressure correlated well with peak ventricular pressure, end-diastolic stretch, ventricular pressure area, and end-diastolic pressure. Of interest was the finding that the same correlation coefficients applied for both end-diastolic stretch and end-diastolic pressure. However, a much higher correlation was obtained using the product of end-diastolic stretch and contractility (defined as the maximum force measured by a strain gauge arch). The conclusion of these studies was that the maximum rate of pressure change is a function of both initial stretch and the contractile state of the ventricle.

Gleason and Braunwald reported on the maximum rate of ventricular pressure change in normal and diseased

humans. They found, as did Reeves, that the maximum value of the first derivative correlated well with peak ventricular pressure and with heart rate. Subjects in failure tended to have a lower maximum rate of pressure change for a given systolic pressure and heart rate. The lack of clear separation of the data, however, indicates that there is insufficient sensitivity of this measurement per se as a determinant of cardiac function.

Volume measurements in the circulatory system - cardiac output and stroke volume - have undergone extensive investigation. Current studies on the relationship of end-systolic volume to end-diastolic volume have shown promise that this ratio provides a sensitive (43) function index

Volume time quotients or rates of ventricular ejection,
which are considered to represent rates of ventricular
fiber shortening, have only recently come under study.

(18)
Braunwald examined the ejection rate in isolated

heart preparations and found that it was increased in normal hearts with augmented stroke volume and heart rate; whereas, in the failing heart where the duration of ejection increased and the stroke volume diminished, the mean rate of ejection decreased. A similar relation—(44) ship was found by Downing and Sonnenblick , who studied the rate of shortening of papillary muscle preparations and found that the normal preparation exhibited no change in fiber shortening rate with an increasing afterload (stroke volume). The measurement of ejection rate thus provides a significant measurement of cardiac performance. The extension of this parameter (36) to the human after exercise has been made by Gorlin

Volume pressure products and their time quotients (cardiac work and power) constitute fundamental performance measurements. However, there is limited usefulness in the independent measurement of these properties, since much overlap exists in the values of work and power both in normal (45) and in pathologic states . But, when compared with an

who related it to the pressure time per beat.

#### 1.20 <u>Use of These Parameters in Estimation of</u> Heart Function

The use of these parameters as independent quantities provides an adequate means of monitoring circulatory activity but does not yield information regarding the functional ability of the myocardium. Measurements of tension time indices, ejection rates, stroke work, etc. so far have shown alterations only in states of advanced heart disease. The value of any of these parameters in distinguishing normal from pathologic function in cases of minimal heart disease has not been demonstrated.

Measurements of cardiac function have been largely accomplished through the use of curves which describe the input-output (e.g. initial tension - stroke work) characteristics of the myocardium in response to stress. The application of such curves to the isolated muscle

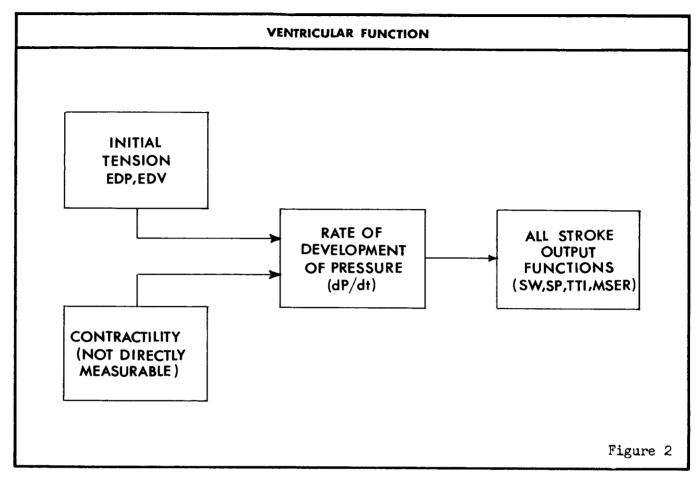
(44) (17)

, heart-lung preparation and the intact has been established. These function human heart curves which are based on Starling's Law of the Heart, state that for a greater initial ventricular tension, a more vigorous contraction must result. Since tension is the product of pressure and radius, both the volume and the pressure in the ventricle must be described to make this measurement. Measurement of the strength of contraction can be made by determining the work performed by the ventricle, or the power generated. Since volume and pressure can vary independently, both quantities must be described to define work or power. The comparison of initial tension and these stroke functions thus describes cardiac function. However, the comparison does not provide for a description of changes occurring in the output of the system in the absence of a change in the input (i.e. changes in stroke work or stroke power without changes in initial tension). This alteration of the intrinsic properties of the myocardium, appropriately labelled "contractility" by Sarnoff , explains the existence of his "families of curves" which describe changing input vs output functions of the heart.

The measurement of cardiac function requires selection of the appropriate input-output hemodynamic parameters for comparison. It has been shown that pressure and volume within the ventricle can change independently (43) because of altered compliance so that neither of these measurements alone would reflect changes in initial tension. However, either pressure or volume has been used successfully in describing cardiac func-(12, 17) tion curves . The output functions, which include dP/dt, stroke work, stroke power, tension time index, initial ventricular impulse, etc. have shown parallel (47) changes under wide conditions .

These relationships can be expressed in the following scheme: (see figure 2)

Immeden.



Initial tension and contractility establish the active state of the muscle which governs the output functions. A comparison of initial tension with the maximum dP/dt (or any other stroke function) will describe contractility, and, therefore, the functional state of the myocardium. This measurement, better than any other, discriminates between a compensating and a decompensating ventricular response to stress. For when an increase in tension fails to achieve a corresponding increase in maximum dP/dt, cardiac decompensation is present.

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### 2.0 <u>Animal Studies</u>

#### 2.10 <u>Introduction</u>

The animal experiments performed during the initial grant period were designed for three specific purposes. These were:

- To define the hemodynamic parameters which distinguish normal from abnormal stress responses.
- 2. To determine the cardiodynamic variables which control the duration of the isometric contraction and ejection periods.
- 3. To provide data for the correlation of vibrocardiograms with multiple hemodynamic parameters under wide physiologic ranges.

To achieve these goals, two types of experiments were developed. The first consisted of acute studies in anesthetized dogs and the second made use of trained animals with implanted cardiac transducers. In both types of experiments, normal and infarcted dogs were utilized.

2.20 <u>Cardiac Function Study -- Methods</u>

The animals in the acute study were dogs whose weights ranged from 20 to 50 pounds. The anesthesia used was nembutal given intravenously, 60 mgm. per kg. Transducer-tipped catheters were passed through the right and left carotid arteries to the root of the aorta and the cavity of the left ventricle, respectively. The femoral vein and artery were cannulated for injection of green dye and sampling of arterial blood for cardiac output determinations. The vibrocardiogram was recorded from the left parasternal area and Lead II of the electrocardiogram was monitored. The following basic parameters were obtained:

- Central aortic pressure via transducer-tipped catheter.
- 2. Left Ventricular pressure via transducer-tipped catheter.
- 3. The Vibrocardiogram
- 4. The Electrocardiogram
- 5. Cardiac output by dye dilution method

In addition, aortic flow was obtained using the method

\*

of Jones et al from the aortic pressure curve and the

first time derivative of left ventricular pressure was

obtained using an operational amplifier.

Thus, in each acute experiment, eight parameters were recorded: vibro, flow, left ventricular pressure derivative, aortic pressure, left ventricular pressure, electrocardiogram and cardiac output. An illustration of these parameters is given in figure 3.

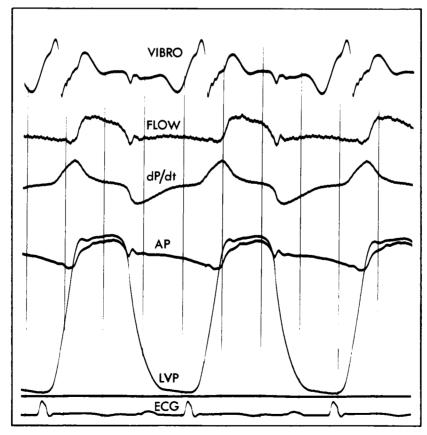


Figure 3

The stress conditions imposed in these studies were as follows:

- 1. <u>Hypoxia</u> Hypoxia was induced by allowing the animal to breathe spontaneously from Douglas bags filled with oxygen and nitrogen gases in three mixtures:
  - a. 15% O<sub>2</sub> 85% Nitrogen
  - b. 10% O<sub>2</sub> 90% Nitrogen
  - c. 7% O<sub>2</sub> 93% Nitrogen
- 2. <u>Hemorrhage and Infusion</u> Rapid expansion or depletion of blood volume was accomplished by infusing or withdrawing 200 300 cc. of blood directly into or from the right atrium through a large bore indwelling cannula.
- 3. <u>Digitalis</u> Rapid digitalization was accomplished by giving 5 mgm. doses of ouabain intramuscularly at 15 minute intervals.
- 4. <u>Isoproteronol</u> This drug was given to simulate some of the cardiovascular effects of exercise \*\*. It was given in an intravenous drip of dextrose and water 0.4 mgm. per liter at a rate of 60 drops per minute for five to ten minutes.

5. Angiotensin This drug was administered in doses of 7 micrograms per kg. per minute in order to provide a pressure load on the cardiovascular system. The use of this drug as a function test has been described by (45)

Cardiac outputs and all other standard procedures for estimating the mechanics of cardiovascular performance were measured as described in section 1.18. These measurements were made before the induction of stress, during stress and after recovery. In four of these acute experiments, infarction was induced by the microsphere technique and response to the same stress was re-examined after infarction.

<sup>\*</sup> Jones, W. B., Hefner, L.L., Bancroft, W.H., Jr. & Klip, W.; Velocity of blood flow and Stroke Volume obtained from the pressure pulse; J.Clin.Invest.; '59,138,2087. 

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2.21 Results

The data obtained in these experiments are presented in Table I, which illustrates the direction of change of these parameters. Although the analysis of these experiments is not yet complete, the data are presented in part to illustrate the difficulties encountered in determining the nature of the ratio response as well as the response of the individual periods to a stress condition. A more complete analysis is now being performed on the determinants of the periods of isometric contraction and of ejection (see section 230).

#### 2.211 Normal Stress Responses

Rapid withdrawal of blood from the right atrium caused a decrease of stroke power, stroke work, stroke volume, derivatives of left ventricular pressure and ejection rate (figure 4). At the same time, the isometric contraction period and ejection periods were both prolonged, resulting in a diminished ratio. Infusion which caused an increase of the stroke functions, (work, power, ejection rate, etc.) caused both the isometric contraction

HEMODYNAMIC RESPONSES TO STRESS

			HEMO	DYNA	MIC	RES	PONSES	TO	STRES
Expt.	IC	EJ	<u>1C</u>	HR	EDF	,	s	MSP	sv

	Expt.	IC	EJ	IC EJ	HIR	EDP	S dP/dt	MSP	sv	MSR	D dP/dt	SW	SP	MER
Hemorrhage	71	+	+	-	-	0	-	-	-	+		-	-	_
	71	+	+	-	-	0	-	-	-	+		-	-	-
	72	+	+	+	0	-	-	-	-	-		-	-	-
	72	+	+	+	+	+	-	-	-	-		-	-	-
	73	0	0	0	0	-	0	-	-	+		-	-	-
	75	+	+	-	0	· -	-	-	-	0		-	-	-
Infusion	71	0	-	+	+	+	+	+	+	-		+	+	+
	71	-	-	-	+	+	+	+	+	-		+	+	+
	72	-	+	-	-	-	+	+	+	-		+		+
	72	-	+	-	-	+	+	+	+	+		+		+
	73	0	0	0	-	+	+	+	+	-		+	+	+
	75	0	0	0	0	+	+	+	+	-		+	+	+
Digitalis	61	-	+	-	-			+	+					
	62	-	+	-	-			+	+					
	63	-	+	-	-			+	+					
	63	+	+	-	-			+	+					
	64	-	+	-	-			+	+					
	72	-	-	0		0	+	+	0	+				+
	73	+	-	+	0	0	+	+	0	0				0
	75	0	-	+	+	0	+	+	-	+				0
	1	-	0	-	0	0	-	0	-		-	-	-	0
	2	-	-	-	+	0	+	+	-		0	+	+	0
	3	-	-	-	+	-	+	0	-		-	0	0	0
	4	-	-	-	+	+	+	-	-		-	0	0	+
	5	-	0	-	+	0	+	+	-		-	-	-	-
	7	-	-	-	+	0	+	+	-		-	-	+	+
	9	-	+		0	0	+	+	0		+	+	+	+
	16	-	-		+		+	+	-		-	+	+	+
Angiotensin	24	+	-	+	0	+	+	+	+	+	+	+	+	+
	30	+	-	+	+	+	+	+	0	+		+	+	+
Exercise	60	-	-	-	+	+								
	60	-	-	-	+	+								
	63	-	-	-	+									
	65	-	+	-	-									
	65	-	-	-	+									
Hypoxia 15%	1	-	0	-	0	-	+	+	-	+	0	+	+	-
	2	0	0	0	0	0	-	-	+	-	-			-
Hypoxia	1	0	+	-	0	0	+	+	-	+	-	-	0	-
	2	0	+	0	+	-		-	-					-
Hypoxia 5%	1	-	+	-	-	0	+	0	0	+	-	0	+	0
	2	-	-	-	+	-	+	-	+		-			+
	3	-	-	-	+	0		-	+	-		0	-	+

TABLE I

Key: IC = Isometric Contraction

EJ = Ejection

HR = Heart Rate

EDP = End-diastolic Pressure

SdP/dt = Systolic dP/dt Max.

MSP = Mean Systolic Pressure

SV = Stroke Volume

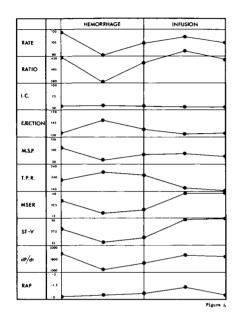
MSR = Mean Systolic Resistance

D dP/dt = Diastolic dP/dt Max.

SW = Stroke Work

SP = Stroke Power

MER = Mean Ejection Rate



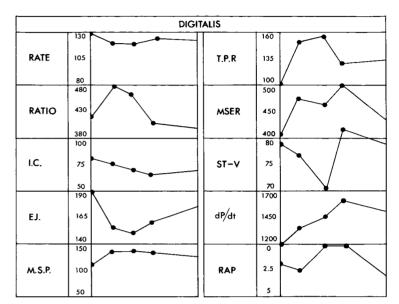
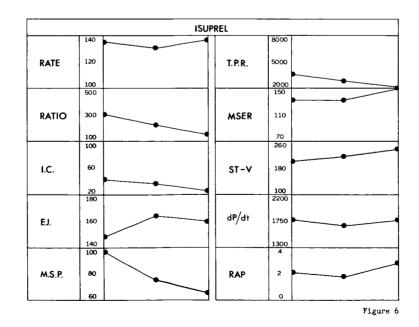
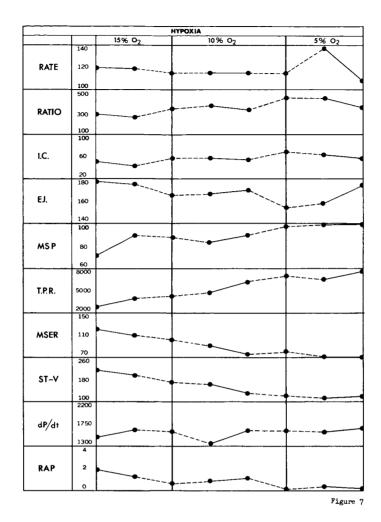
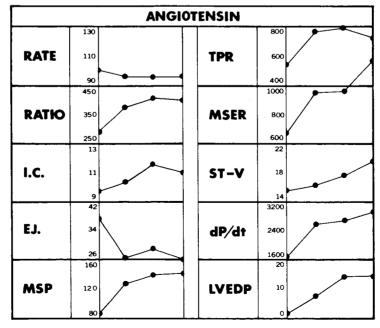


Figure 5



Lummer





and the ejection periods to shorten (figure 4). The ratio again diminished because the isometric contraction period shortened to a greater extent than the ejection period. The heart rate responses for both hemorrhage and infusion were variable.

The administration of <u>digitalis</u> (figure 5) caused an increase in both stroke volume and mean arterial pressures and, also, the resultant work and power functions. Isometric contraction was diminished and ejection prolonged resulting in a diminished ratio.

The heart rates tended to be diminished with digitalis administration and end-diastolic pressures showed no change.

Isuprel infusion caused an increase of the stroke functions which included stroke volume, arterial pressure, stroke work and power, and ejection rate (figure 6). The isometric contraction period was consistently shortened as was the ejection period. The ratio, however, was again diminished in all cases while heart rate tended to increase and end-diastolic pressure remained the same.

The hemodynamic responses to various levels of <a href="https://www.hypoxia">hypoxia</a>
(figure 7) were quite variable, but the isometric contraction/ejection ratio was diminished in all cases.

The experiments performed with <u>angiotensin</u> (figure 8) showed an increase in all of these stroke functions with a corresponding increase of isometric contraction time and a decrease of ejection time which resulted in an increased ratio.

Of all these stress states studied in the normal dog, the response to angiotensin was the only one in which an increased ratio was observed. In all of the other conditions, the responses of the individual periods of isometric contraction and ejection were variable. The resultant ratio, however, was always diminished.

## 2.212 Normal vs Post Infarction Responses to Isuprel and Angiotensin

In certain experiments, animals were infarcted by the microsphere technique and their responses to stress examined in the normal and infarcted state. In these experiments, it was desired to perform a more complete

analysis of the data. All possible parameters of function were, therefore, measured (see section 1.18). These data are presented in Tables 2 and 3, and graphically illustrated in figures 9 and 10.

With the administration of isuprel (figure 9), cardiac output, mean ejection rate, stroke work, stroke power, stroke volume, heart rate and maximum systolic pressure derivative were all increased. Systolic resistance and the diastolic pressure derivative were diminished. The isometric contraction period was diminished, and the ejection period was slightly increased resulting in a diminished ratio.

The immediate changes as a result of embolization with microspheres were decreases in cardiac output, ejection rate, stroke work, stroke power and stroke volume, while isometric contraction time and ejection time increased. The response to isuprel after infarction, however, was again the same as noted before infarction: cardiac output, ejection rate, stroke work, stroke power, and stroke volume were all increased. The period of

15119

SdP/dt DdP/dt	2310 1580	2890 1360	3350 1400	3080 1570	2790 1450		1350 802	1750 1050	1610 960	EMI - Electro Mechanical lag (secs) COT - Electron (secs) COT - Electron (secs) IN - Elecertic (secs) D - Disatole (secs) RR - Cycle length (secs) RR - Heart Mate (beats/min)
dPS q	25.6 2	27.8 2	39.8	23.7 3	25.7 2		32.7	38.0	36.4 1	Electro Mechanical Lag (secalization (secalization) (secalization) (secalization) (secalization) (secalization) (secalization) (secalization) (secalization) (secalization)
o	200.1	141.0	147.0	201.0	199.0		183.0	120.0	110.0	Electrical
æ	38.4	24.2	29.7	45.6	6.44	NOIL	56.5	21.6	20.2	
¥	28.0	12.3	11.4	22.8	23.1	POST INFARCTION	32.0	14.3	8.01	6) iig-secs) iig-secs) niig-secs)
MEAN	117	76	86	127	125	PO	\$	81	75	uhg) nig) mmhg-sec mmhg-sec krea (mm kr
DIAS-P	106	85	85	118	112		78	62	28	issure (an immig) is (ammig) is (ammig) is a Ara (in ressure in ressure dt (ammig) if (a
SYS-P	124	103	112	140	132		86	86	81	Pressure Pre
EDP	0	0	2	0	0		0	0	0	End Disatolic Pressure (mmig)  Systolic Pressure (mmig)  Disatolic Pressure (mmig)  Hean Systolic Pressure (mmig)  Ilometric Pressure (mmig, secs)  Ilometric Reiss Pressure Area (mmig-secs)  Static Election Pressure Area (mmig-secs)  Dynamic Election Pressure Area (mmig-secs)  Punnant Election Pressure Area (mmig-secs)  Static Disatolic dP/dt (mmig/sec)  Stroke volume (min)  Stroke Volume (min)  Stroke Work (1-mmig)  Stroke Work (1-mmig)  Stroke Work (1-mmig)
	rol	10' Isuprel	10' Isuprel	15' Recov	15' Recov		rol	10' Isuprel	10' Isuprel	EDP SYS-P DIAS-P MEAN A A B B B B B B C C C C C C C Sy Sy Sy Sy Sy Sy Sy Sy Sy Sy Sy Sy Sy
	Control	10,	10	15,	15'		Control	10	10	Key:

TABLE IIa

SUPREL

	SV	8	MER	AS.	SP	MSR	E C	ICI	ECT	H	۵	R-R	- 1
Control	18.1	2.26	938	21.3	110	645	32	79	193	45	176	411	
10' Isuprel	20.8	3.06	1210	19.8	115	450	78	87	172	47	165	412	
10' Isuprel	24.2	3.46	1370	23.7	134	405	78	95	177	47	160	420	
15' Recov	21.0	2.78	1180	26.7	150	909	56	89	178	65	183	757	
15' Recov	21.2	2.17	1200	26.6	150	290	53	69	176	28	176	760	
					POST	INFARCTION	NOI						
Control	13.9	1.25	620	13.0	59	675	29	105	223	63	310	999	
10' Isuprel	15.6	1.92	840	13.6	73	520	31	09	186	20	206	485	
10' Isuprel 19.4 2.39	19.4	2, 39	1020	14.5	9/	396	25	62	161	84	204	483	

126 146 143 132 130

TABLE IIb

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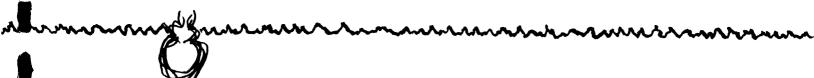
#### ANGIOTENSIN A

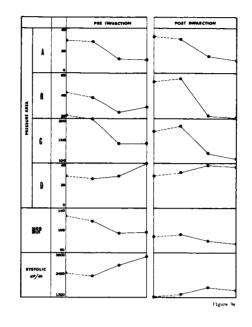
(Do	og 30)									
						LV R <b>EA</b> S			s	D
	EDP	SYST.	DIAST.	MEAN	A <sub>mm</sub> 2	B <sub>2</sub>	С	D	dP/dt	dP/dt
Control	3.1	93	70	88	10.3	22.6	126.2	24.1	2730	1620
3'ANG	6.2	140	118	136	16.4	29.4	160.4	15.0	4100	
5 ' ANG	7.7	156	134	142	19.7	31.9	161.0	16.7	5200	2480
10' ANG	8.5	173	150	168	21.8	44.1	180.9	16.0	5450	2720
1'RECOV	7.7	154	132	150	18.6	28.6	174.7	19.9	4600	
5'RECOV	7.7	110	82	104	19.0	25.2	129.8	27.3	3200	1740
				POST	INFARCT	ON				
Control	15.5	87	47	79	7.8	21.2	62.5	64.7	1740	1000
3 ' ANG	15.1	106	65	98	10.1	27.2	74.8	42.1	2730	1730
5 ' ANG	17.8	100	65	93	11.8	27.7	82.6	40.4	2730	1750
10 ' ANG	19.4	100	76	95	13.6	30.2	80.6	44.1	2200	1730
4'RECOV	18.6	98	55	89	11.2	16.8	79.9	64.2	1866	1220
				T	ABLE III	ì				

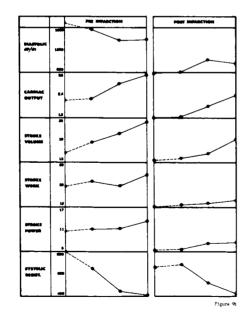
ANGIOTENSIN B ANGIOTENSIN C (Dog 30) (Dog 30) sv CO MER SW SP MSR EML ICT ECT IR D R-R HR Control 1.45 Control 021 3 'ANG 1.58 3 'ANG 5 ' ANG 1.85 5 'ANG 10'ANG 1.85 10'ANG 1'RECOV 1.80 1'RECOV 020 5 'RECOV 1.54 5'RECOV POST INFARCTION POST INFARCTION Control 1.24 Control 025 3 ' ANG 3 'ANG 5 'ANG 1.50 5 'ANG 10' ANG 1.32 10'ANG 4 'RECOV 4'RECOV 017 0.98 

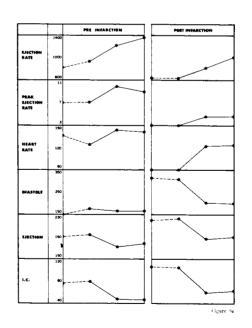
TABLE IIIC

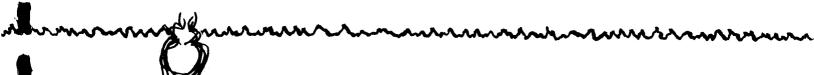
TABLE IIIb

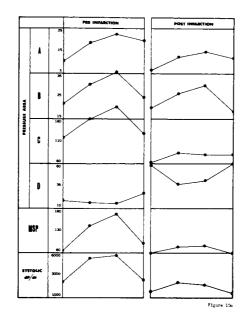


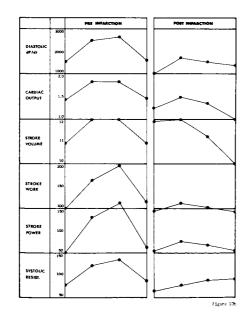


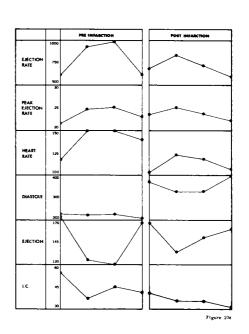












isometric contraction was again diminished as was the ejection period. Systolic resistance showed the same decrease both before and after infarction and heart rate was increased in both states. The areas under the ventricular pressure curve all showed decreases with isuprel before and after infarction, save area D, which increased in both cases. Mean systolic pressure was diminished both before and after infarction.

In summary, none of the single parameters measured in these experiments showed differences between normal and infarcted dogs after the administration of isuprel.

The response of a normal and infarcted dog to angiotensin is illustrated in figure 10. As will be noted, cardiac output, ejection rate, stroke work, stroke power, stroke volume all increased after angiotensin as did the pressure areas A, B, and C. Pressure area D diminished as it did with isuprel. Mean systolic pressure, however, was increased with angiotensin. Both systolic and diastolic pressure derivatives showed increases along with increases in systolic

resistance but little or no change in heart rate. The isometric contraction period was prolonged, and the ejection period markedly shortened resulting in an increased ratio. The same observations were found after infarction upon administration of angiotensin.

These results indicate that none of the cardiovascular parameters, used by themselves, indicate states of dysfunction. This is well documented by the fact that cardiac output, stroke volume, stroke work and stroke power were all increased with stresses both before and after infarction. The only parameter which was directionally different in the infarcted dogs was the maximum value of the diastolic pressure derivative which was increased in the infarcted dog after isuprel and diminished in the normal dog. This finding is now being examined further. Since transaminase elevations and autopsy showed that the animals were infarcted, it appears that either there are no differences in these hemodynamic parameters as tested, between the normal and infarcted dogs, or that the conditions did not

impose sufficient stress, or that the proper factors were not examined.

2.213 Normal vs Post-Infarction Function Curves

Since the independent examination of the cardiac parameters did not discover differences between normal and infarcted dogs, an examination was made of the interrelationships between certain of these functions. A total of 23 dog experiments were examined. Nineteen of these were normal and 4 were post-infarction animals.

Of the 19 normal experiments, 7 tested the effects of isuprel; 5, hypoxia; 2, the effects of digitalis; 2, the effects of rapid infusion; and 2, the effects of angiotensin. In the 4 post-infarction studies, isuprel was administered in 3 and angiotensin in one. The significant parameters from the previous studies were chosen as follows:

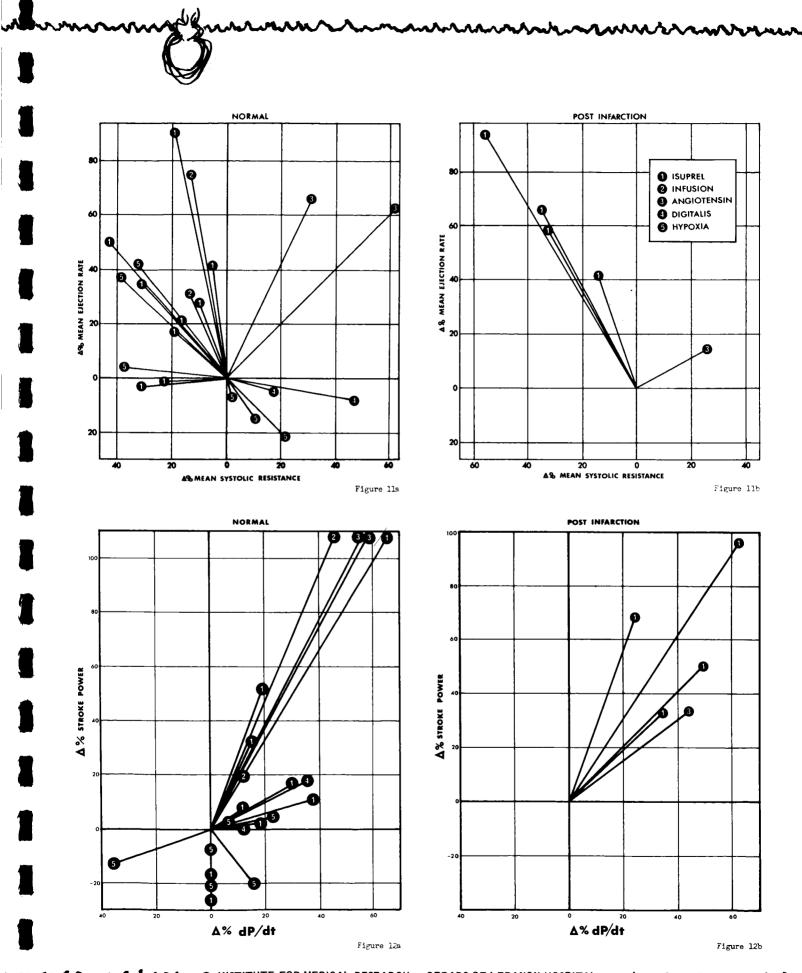
- 1. systolic dP'dt
- 2. mean ejection rate
- 3. mean systolic resistance
- 4. stroke power

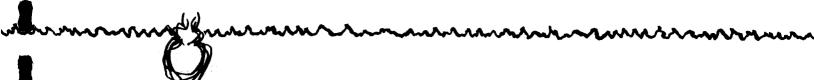
In figure 11a, effects of these stresses on mean ejection rate and mean systolic resistance is presented. As will be noted, all stresses except angiotensin caused either increases in ejection rate with decreases of systolic resistance or decreases of systolic resistance with increased ejection rates. The possible interpretation of this chart is that none of the tests except angiotensin imposed a real stress, since whenever an increase in ejection rate was encountered, a corresponding decrease in resistance was found. With angiotensin, however, there were increased ejection rates with increased systolic resistances. In figure 1lb, the response of the infarcted animals is illustrated. As will be noted, no differences can be seen between normal and infarcted dogs with perhaps the exception of the angiotensin experiment, which does not show directional differences but does show a lesser increase than in the preinfarction state.

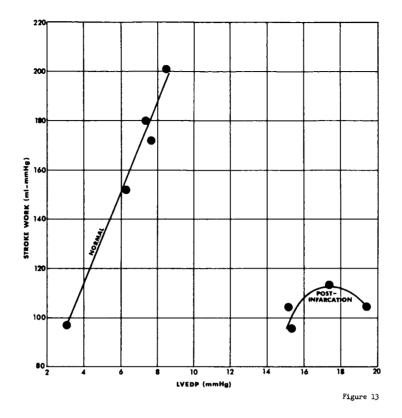
In figure 12a, is illustrated the per cent change of the stroke power index vs systolic pressure derivative. Again,

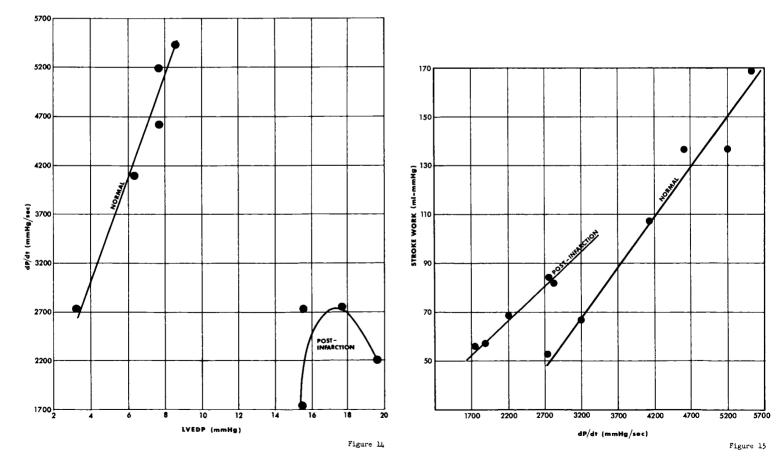
nearly all conditions fall in quadrant one which indicates an increased stroke power with an increased systolic dP/dt. The same conditions were true after infarction, figure 12b.

Since neither of these presentations again served to differentiate normal from infarcted states, a further function presentation was made which utilized the inputoutput relationships as outlined in section 1.20. Figure 13 illustrates the left ventricular end-diastolic pressure vs stroke work. As will be seen, the normal dog shows a linear increase of both quantities whereas, after infarction, a descending limb of the function curve is described. The same result can be achieved by plotting the left ventricular end-diastolic pressure against the systolic dP/dt. Here, a more clear definition of the state of decompensation is noted (figure 14). A comparison of the stroke output functions, however, yields identical responses for both normal and post infarction conditions (figure 15).









2.22 Conclusions of Cardiac Function Experiments
Examination of single parameters does not distinguish
normal from pathologic responses to stress. In order
to demonstrate cardiac decompensation, the inputoutput (Starling) response must be examined. This may
consist of relating initial tension (or any other
input function) to a stroke output function such as
dP/dt, stroke work, or stroke power. In addition,
the induced stress must be such as not to alter the
contractile state of the myocardium while increasing
its initial tension. These conclusions are illustrated
in the scheme outlined in figure 2 (page 34).

Initial tension and contractility both govern the rate of tension development which in turn governs all other stroke output functions. In order to define changes in contractility (the term which indicates the functional state of the myocardium) initial tension and an output function must be presented. Any changes which occur in the stroke output functions without alterations

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in initial tension can be ascribed to an altered contractility. The objective of a stress test is to test contractility; therefore, the stress must be one which does not alter the intrinsic properties of the myocardium. Such is the case with a peripheral acting drug (angiotensin) while with the central acting drug (isuprel) abnormal function could not be exhibited.

# 2.30 <u>Determinants of Isometric Contraction and</u> Ejection Time

Because of the value of the isometric contraction/
ejection time ratio in discriminating normal from
coronary insufficient subjects (see Progress Report,
NsG289-62, pp.85-90), it was desired to establish
the manner in which cardiodynamic variables control
these two phases of the cardiac cycle. Previous
studies on the duration of cardiac events have indicated
\*
that heart rate is a major determinant of their duration .

In the present experiments, the effects of stroke volume, systolic pressure, and rate of pressure change on these periods are being compared with the effects of heart rate.

<sup>\*</sup>Weissler et al; Messer et al, (NsG289-62 p.92)

It will thus be possible to determine the relative importance of each of these parameters in the control of cardiac events.

The factors acting during isometric contraction are:

1) the initial tension of the ventricle, 2) the

contractility of the ventricle, and 3) aortic diastolic

pressure. Because it is not possible to measure con
tractility directly, the maximum rate of intraventri
cular pressure change was used to indicate the combined

effects of the contractile state and initial tension.

For the ejection period, three primary determinants

were chosen: 1) the maximum value of the rate of intra
ventricular pressure change, 2) the stroke volume, and

3) the systolic pressure.

The combined effects of these factors on the isometric contraction and ejection periods are diagramatically presented in figure 16 and a preliminary regression analysis illustrated in figure 17. A more extensive analysis on the determinants of these periods is now being undertaken.



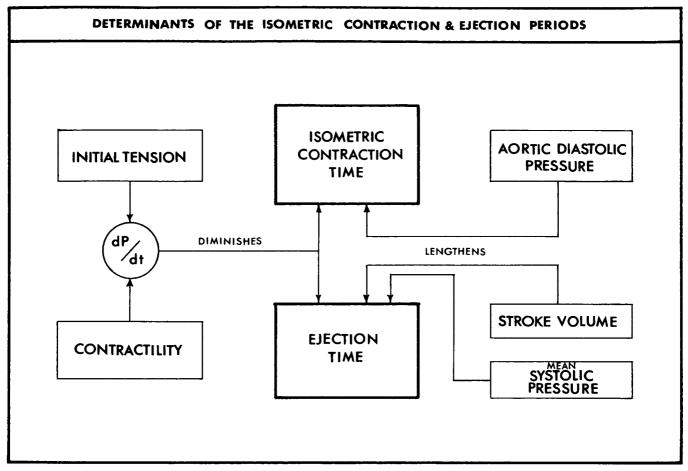
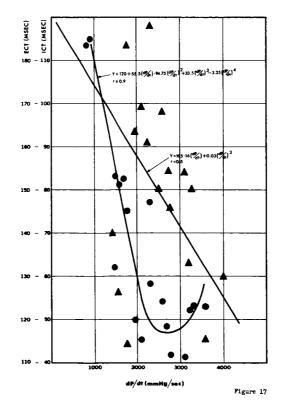


Figure 16



2.40 <u>Electropressor Latency Period Studies</u>

The electropressor latency period (EPLP) has been studied in animals in order to determine whether this interval can be used as an indicator of myocardial function. This period represents the time between the onset of electrical excitation and mechanical response of the ventricle.

#### 2.41 Methods

There are three methods by which this interval can be measured; the first is the onset of the QRS complex to the H wave of the vibrocardiogram, the second is the onset of the QRS complex to the first rise in intraventricular pressure, and the third is the onset of the QRS complex to the first motion of either a strain gauge or a mercury plethysmograph attached to the ventricle. These methods are indicators of two distinct phenomena. The first is the initial motion of the ventricle which is indicated by the deflection of a strain gauge attached to the ventricle and also the vibrocardiographic H wave. The second event is the first pressure

rise in the left ventricle, which necessarily follows the first ventricular motion but marks the onset of isometric contraction.

Thirteen experiments have thus far been studied. These include 5 hypoxia studies, 10 isuprel studies, 3 infarction studies, 3 digitalis studies and 1 hemorrhage study. The measurements included the QH interval, the QR interval, the Q to the onset of left ventricular pressure rise, and Q to the onset of the first heart sound.

## 2.420 Results

The changes in the EPLP are discussed below.

#### 2.421 Isuprel Studies

Six experiments were studied in which isuprel was administered. The interval between Q and the onset of left ventricular pressure averaged about 25 MSEC, with a range of 20 to 40 MSEC (Q-LV). After the administration of isuprel, the range was unchanged. The mode value for control was approximately 25 MSEC and was the same after

administration of isuprel. In 2 experiments there was a shortening of the Q-LV interval. In one experiment this interval remained the same, in 2 experiments it was increased. The changes in the Q-LV interval were less than 10 MSEC and in most cases were of the order of 2 to 3 MSEC. These time differences are beyond

the measurement limitations of this report.

In 9 experiments the interval between the R wave and the onset of left ventricular pressure rise was measured. In 5 of these experiments the R-LV interval diminished, in 2 it increased, in 2 it remained the same. The range of the controls was -2 to +8 MSEC, and it was approximately the same after administration of isuprel. It is concluded, therefore, that the administration of isuprel does not significantly alter the EPLP.

The finding that the R-LV interval in 7 of the 9 experiments fell within 7 MSEC, serves to substantiate the previous finding that the R wave of the ECG in animals can be used to identify the onset of left ventricular

pressure rise, and hence the onset of isometric contraction.

## 2.422 <u>Hypoxia Studies</u>

The EPLP in the control state ranged from 29 to 35 MSEC, the average is about 32 MSEC. After various degrees of hypoxia ranging from 5% O<sub>2</sub> to 15% O<sub>2</sub>, the EPLP range was 28 to 39 MSEC, and the average was again about 32 MSEC. The greatest changes encountered in any single experiment were on the order of 5 to 6 MSEC and, therefore, probably not significant.

In one experiment, however, the dog was given 5%  $O_2$  for a period of 23 minutes. In this experiment there was a change of the EPLP from 32 to 39 MSEC. This is the only experiment in which a significant change occurred, and is consistent with the hypothesis that the EPLP is prolonged in states of dysfunction.

The R-LV interval showed slight variation ranging in the control state from -5 to + MSEC with approximately the same range with induction of hypoxia. None of the experiments are considered to have significant changes in the R-LV interval. However, it is significant to note that

the R-LV interval is again within the plus or minus 10 MSEC limit, with 7 of the 9 cases falling within  $\pm$  5 MSEC.

## 2.423 <u>Embolization Studies</u>

Three dogs have thus far been studied after coronary embolization. In two of these dogs, left ventricular pressure measurements were obtained. In 2 animals the changes in the EPLP were not considered significant, 1 changing 3 MSEC and the other not changing.

## 2.424 Digitalis Studies

Observations were made in three experiments in which digitalis was given. In these three experiments the EPLP was shortened after administration of digitalis. In two of these experiments the shortening was of the order of 2 to 3 MSEC, and in one experiment there was approximately a 10 MSEC shortening of Q-LV interval.

## 2.425 <u>Hemorrhage</u>

Observations were made on the EPLP in 2 dogs after rapid withdrawal of blood and rapid infusion of blood.

In both cases the EPLP was prolonged after withdrawal of blood and was again returned to control levels after infusion. The changes ranged from 3 to 12 MSEC in these experiments and, therefore, border on being significant.

## 2.43 Discussion

The EPLP has been considered as one measure of myocardial function. It was assumed that this interval would be shortened under stress conditions in the normal heart and prolonged in the abnormal heart.

In these experiments, changes in the EPLP were slight with only a few measurements bordering on significance. Directionally, the changes were as expected. With administration of digitalis, isuprel, the interval was shortened; with hypoxia there was slight prolongation of the interval, as there was with hemorrhage. There is one factor, however, which must be considered in evaluating the data. The physiologic states associated with dysfunction are those in which ventricular pressure is generally of low magnitude. There may be a much greater error in locating the onset of left ventricular pressure rise in these

conditions than in the control state. This may explain why the EPLP is prolonged under conditions in which pressure is diminished.

#### 2.44 Conclusion

It is concluded that the EPLP does not provide a practical measurement of cardiac function. The changes in this interval after hypoxia, infarction, etc., are slight and probably outside the measurement capabilities of the equipment. It is also noteworthy that the electromechanican lag period occupies only a small portion of the cardiac cycle, -4% to a maximum of 10%. In the light of these factors, the electromechanical lag period may have questionable significance.

# 2.50 <u>Vibrocardiographic Area Studies</u>

The method of evaluation of cardiac function, as determined both through experimental studies and a literature survey is dependent on obtaining an index of initial ventricular tension as well as determination of a stroke output function. Through the analysis of the determinants of isometric contraction time, (see section 2.30), it is

hoped to be able to predict the maximum value of dP/dt, thus satisfying the output function requirement. An index of initial ventricular tension, however, has not yet been formulated. It was thus desired to obtain a factor from the vibrocardiogram which represented initial ventricular pressure, volume, or tension. The observation that the vibrocardiogram resembled a time derivative of intraventricular pressure and circumference led to the study of integrated vibrocardiograms in order

#### 2.51 Methods

to estimate these properties.

For these studies, use was made of the intact animal exercise data in which simultaneous vibrocardiograms and ventricular mercury plethysmograms were recorded under a variety of ventricular volumes (figure 18).

Using these data, it was possible to achieve a reliable measurement of ventricular end-diastolic volume. The vibrocardiograms were integrated in the region of diastole. Since the value of the integral is dependent on the boundary values chosen, four different

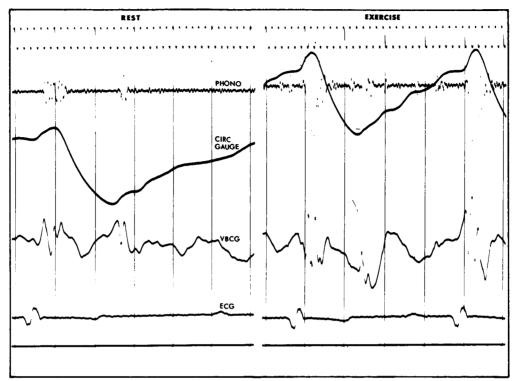


Figure 18

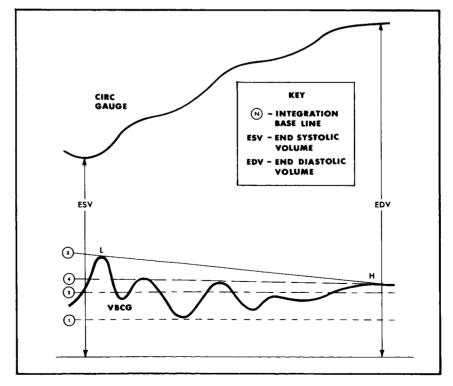


Figure 19

baselines were selected and the areas obtained by each compared to the mercury gauge data (figure 19). These baselines are described as follows:

- A line connecting the lowest points of the vibrocardiogram in the diastolic area in two successive beats.
- 2. A line connecting the intercept of the nadir of the strain gauge curve and vibro in two successive beats.
- A line connecting the vibrocardiographic
   L and H waves.
- 4. A line connecting H waves in two successive beats.

#### 2.52 Results

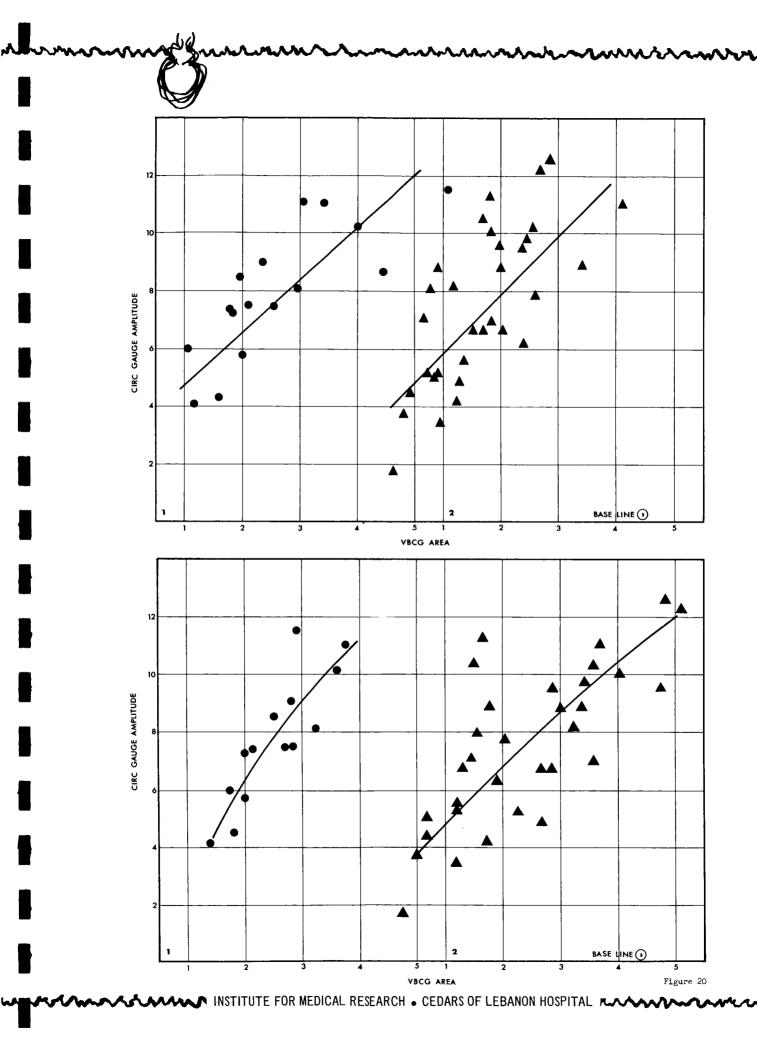
The data obtained in a preliminary analysis of two experiments are presented in Table V and illustrated in figure 20.

The use of baselines 1 and 3 provided a good correlation with end-diastolic volume in both experiments, while baseline 2 showed some correlation but a great degree of

# VbCg Integration Data

Circ. Gauge					
Amp1	1	2	3	4	(Baseline)
58	255	200	200	358	-
74	612	250	262	482	
88	763	440	545	808	
115	1121	555	645	904	
43	160	157	180	144	
73	415	178	203	176	
91	583	235	272	230	
110	671	338	371	326	
41	120	116	134	70	
72	248	180	200	153	
86	450	194	245	239	
115	550	306	<b>2</b> 85	<b>2</b> 78	
60	137	109	166	76	
74	260	211	271	105	
81	367	<b>2</b> 90	325	120	
102	505	393	355	136	

TABLE IV



scatter. Baseline 4 showed little correlation.

While these studies represent only pilot experiments, they do indicate that a measurement of ventricular end-diastolic volume may be achieved using the vibrocardiogram. Further experimentation using these methods will be performed. Should such measurements prove to be reliable, the vibrocardiogram will provide a significant means of monitoring cardiac function as well as performance.

## 2.60 Chronic Animal Study

A series of experiments was undertaken to determine the effects of exercise in trained, intact animals (figure 21). In certain of these experiments, mercury gauges were attached circumferentially about the left ventricle. The use of this device permitted the determination of stroke volume, end-diastolic volume, end-systolic volume, fiber shortening rate, and identification of cardiac phases. These means by which these parameters are measured is shown in figure 22. In several of these studies, the animals were infarcted by coronary ligation at the time of implantation.



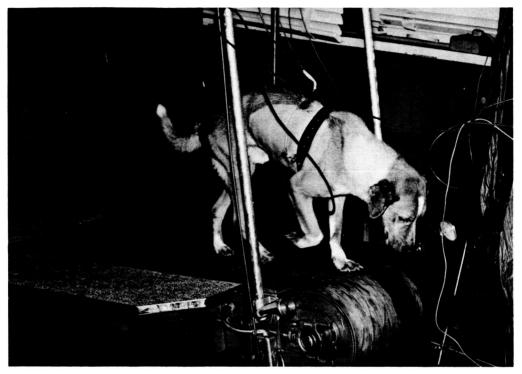


Figure 21

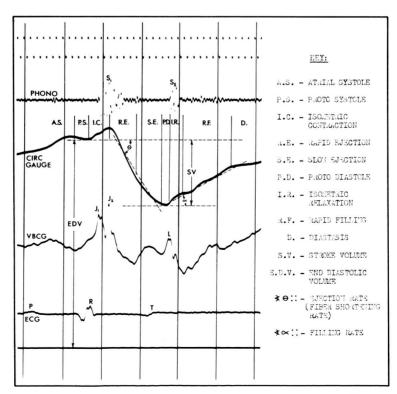


Figure 22

Analysis of the data from these experiments has recently been initiated to define the following areas:

- 1. The correlation of VbCg with cardiac events, particularly the diastolic phase (rapid and reduced filling) whose definition is not possible with ordinary cardiac pressure curves.
- The contrast of hemodynamic responses to exercise and posture change in normal and infarcted animals.
- 3. The correlation of VbCg with enddiastolic volume, stroke volume, fiber shortening rate, etc.

## 3.0 <u>Human Studies</u>

#### 3.1 <u>Introduction</u>

Exercise testing of normal and coronary insufficient subjects has continued in accordance with the proposed research program. Two types of tests have been employed in the current series of subjects. These were the treadmill and the Master 2-Step tests.

The treadmill test was employed to achieve a more uniform level of exercise and to provide a higher level of exertion than available with the step test. This test is especially useful, because much data regarding heart rate, blood pressure and oxygen consumption are already available.

The step test was used as a means of comparing the standard electrocardiographic response with the exercise vibrocardiogram and also served as a means of evaluating subjects who were unable to achieve even the first level of treadmill exercise. The following methods and procedures were used during these forms of exercise testing.

3.20 <u>Methods - Exercise Testing</u>

## 3.21 <u>Treadmill Exercise</u>

The treadmill exercise test consisted of walking on a 10% grade at a speed of 1.73 miles per hour for 10 minutes. This test has been described previously (23) by Bruce and was chosen as it provides a submaximal exercise level which is applicable to both normals and subjects with coronary artery disease. A second exercise level was also established for those patients who were able to complete the first exercise level without developing symptoms. This level consisted of walking on a 10% grade at 3.46 miles per hour for 10 minutes.

The parameters recorded during these procedures included the vibrocardiogram, electrocardiogram, blood pressure and oxygen uptake. The tests were performed in the following manner: each subject rested in a supine position at least 15 minutes before the test. During this time the blood pressure, vibrocardiogram and electrocardiogram were recorded.

The subject then stood on the treadmill for a period of four to six minutes, during which time the oxygen uptake, vibrocardiogram, electrocardiogram and blood pressure were recorded. During the course of exercise. the subject maintained respiration through the gas analysis system so that this system was constantly flushed with the expired air. Minute samples of expired air were collected at the fourth to fifth minute of exercise. At the fifth minute of exercise, after the oxygen sample had been recorded, the treadmill was momentarily stopped so that vibrocardiograms and electrocardiograms could be recorded. The vibrocardiographic data at the tenth minute of exercise were recorded immediately after the treadmill stopped. Records were then taken at the first, second, third, fifth, tenth and fifteenth minute of recovery. A final oxygen sample was recorded during the fourteenth to sixteenth minute of recovery. Recordings of electrocardiograms and vibros were also obtained at one minute increments during exercise. These were obtained so that the precise appearance of an ischemic

ST segment change in the abnormal subjects could be determined.

## 3.22 <u>Master 2-Step</u> Test

The standard Master 2-step test was utilized in these studies. Both single and double tests were performed. The parameters studied included heart rates, blood pressures, electrocardiograms and vibrocardiograms. Records were obtained before, immediately upon completion of the test and after five minutes of recovery.

## 3.23 <u>Methods of Data Analysis</u>

The oscillographic records containing the vibrocardiograms and electrocardiograms from the Master test exercise studies were measured without the aid of data processing equipment, and the following calculations made: The  $R-J_2$  interval, the  $J_2-L$  interval, the R-R interval.

A more sophisticated approach to data analysis was attempted for the treadmill exercise data. For these

1 Ommenden mannemander 1

studies, it was desired to establish automatic data processing methods so that the vibrocardiographic traces would be automatically measured and the data stored in digital form for further use. procedure involved digitizing the vibrocardiograms utilizing optical equipment and establishing programs to calculate the various interval ratios and blood pressure and heart rate measurements. This program was initiated so that more accurate measurement of the interval ratios could be achieved and also because this method provides a means of readily storing the vibrocardiographic data in a form which can easily be subjected to other forms of analysis. These include integration (areas under various portions of the curve), spectrum analysis and other forms of complex wave form analysis. The method by which the oscillographic charts were read is presented in section 4.10.

# 3.24 <u>Classification of Subjects</u>

The following criteria were established for classifying

the subjects of the exercise test and the criteria for a positive electrocardiographic exercise response is also presented.

#### CLINICAL CLASSIFICATION

## IA Normals 55 years or under

#### IB Normals over 55 years

No history of chest pain suggesting coronary disease.

No cardiac findings on physical examination.

No hypertension, thyroid disease, diabetes, etc.

No abnormal ECG changes at rest or during exercise.

No cardiac enlargement.

#### IIA Functional Normals 55 or under

#### IIB Functional Normals over 55

Clear-cut history of myocardial infarction or previous angina pectoris but:

No present chest pain.

No restriction of activity.

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## Subgroups:

- 1. No abnormal cardiac findings.
- Cardiac enlargement, abnormal resting ECG,
   Grade III murmur, etc.
- Ischemic ST segment depression on exercise but no symptoms.

#### IIIA Abnormals 55 years or under

#### IIIB Abnormals over 55 years

Clear-cut history of myocardial infarction and angina on ordinary activity.

Must be restricted in some degree by <a href="https://example.com/chest-pain">chest pain</a>, dyspnea, palpitation, etc.

#### Subgroups:

- 1. No abnormal cardiac findings.
- 2. Cardiac enlargement, abnormal resting ECG, Grade III murmur, etc.
- 3. ST segment depression on exercise.

## IVA Miscellaneous 55 years or under

## IVB Miscellaneous over 55 years

- 1. Hypertension
- 2. Thyroid disease

- 3. Valvular disease
- 4. Pericarditis History
- 5. Right Bundle Branch Block only abnormality
- 6. Left Bundle Branch Block only abnormality
- 7. Abnormal resting ECG
- Positive 2-step test no chest pain on exertion.
- Indeterminate, particularly undiagnosed chest pain.
- 10. Heart Block
- 11. Myocarditis
- 12. Diabetes

## Criteria for Evaluation of ECG'S

Positive Pathological Response:

Distinct depression of J point followed by

an RS-T segment that continues straight

for at least 0.08 seconds or dips.

A negative U wave provoked by exercise.

Appearance of second or third degree

A-V block.

Developing bundle branch block.

Appearance of severe ventricular arrhythmia.

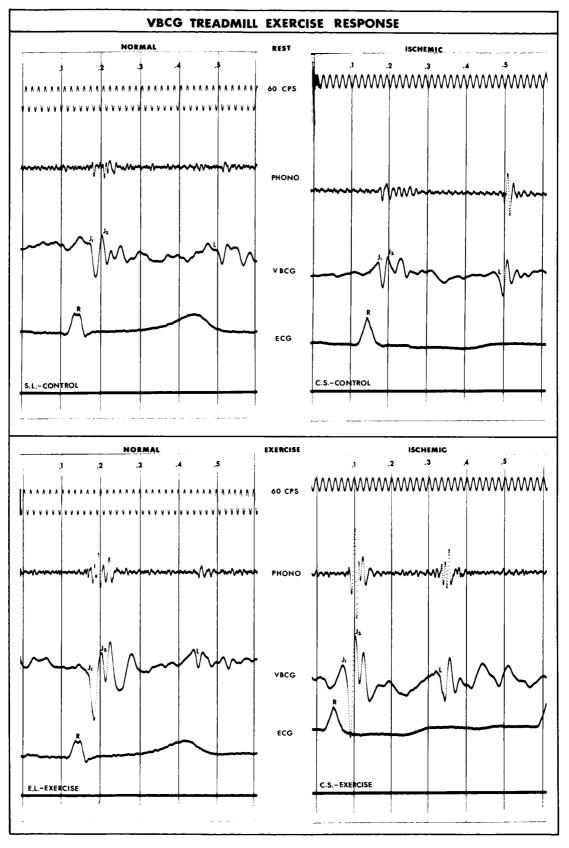
## 3.30 Treadmill Results

The data obtained from the treadmill studies are presented in Tables V, VI, VII, VIII and typical records illustrated in figure 23. The following observations were made:

#### 3.31 Oxygen Uptake Measurements

The oxygen consumption values for the normal and abnormal groups are illustrated in figure 24. At rest, both normal and pathologic subjects have essentially the same oxygen uptake. During the first level of exercise, the ischemic subjects had a slightly higher oxygen uptake than the normals, but the mean values for each of the groups are within one standard deviation and, therefore, not considered significant. During the ninth to tenth minute of exercise, the ischemic subjects exhibited a further increase in mean oxygen uptake, whereas the normal subjects remained the same. The mean values at the last minute of exercise still fall within one standard deviation, and the fifteen minute recovery oxygen values were practically the same for both groups.

S.



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OXIGEN UPTAKE
ML/Min/Meter<sup>2</sup>
(heats/min)

ML/Min/Meter <sup>2</sup>							(bests/min)												
	NORMAL							NORMAL											
	1 Std	1 Ex 4/5	1 Ex 9/10	1 Rec 15	2 Ex 4/5	2 Ex 9/10	2 Rec 15												
_									C	1 0+4		1 Ex		l Rec	2 624	2 Ex		2 Rec	
В.	168.4	619.3	379.9	174.7	468.3	616.7	209.0		Sup	1 Std	4/5	9/10	3	15_	2 Std	4/5	9/10	_3_	_15
T.B.	167.6	613.3	591.2	181.7	1006.0	925.2	194.7	D.A.	62,2	67.7	94.0	106.0			04.0	***			
M.D.	180.2	584.1	604.1	126.4					02.2	101.3		106.0	87.3	86.9		135.8			103.1
T.F.	142.6	441.6	522.5	125.2	698.7	711.4	150,7	В.						97.5		134.3			98.5
W.H.	137.4	499.8	535.0	166.5	1086.5	1014.0	153.8	Т.В.	63.3		81.5	84.8	66.1	67.5	67.5	100.8	106.6	73.5	66.9
I.H.	192.7	663.7	690.2	302.5				M.D.	64.5	83.0		87.6	84.5	81.1					
M.L.	170.9	574.8	529.5	140.3	1219.7	1154.6	153.3	T.F.	85.8	97.4		109.6	100.1	98.5	98.5			107.6	96.4
E.L.	160.4		754.9	151.4				W.H.	64.9	80.0			98.0	91.7	91.7	136.0	133.6	106.4	93.3
C.L.	147.2	673.4	605.3	135.0	1023.7			1.H.		77.4		108.4	82.0	83.1					
L.L.	126.5	529.4	595.9	128.5	857.6	862.2		M.L.	79.5	99.8	111.6	113.9	102.4	97.2					
A.S.	164.0	558.8	558.7	138.9	983.6	876.6	172.2	E.L.	46.0	52.0	67.3	62.6		49.0					
R.S.	190.4	654.4	714.4	227.4	975.4	1088,3	218.0	C.L.	58.1	57.0	98.8	95.6	62.3	62.6		112.7			
H.T.	135.1	612.6	740.3	148.2	1002.2	850.7	142.7	L.L.	64.0	63.4		107.0	84.8	70.8	70.8	120.5	138.3	104.4	87.4
H.W.	135.4	421.9	407.0	159.9	885.5	837.7	152.8	A.S.	55.2	92.8	80.8	90.9	69.5	80.3	80.3	121.7	126.6	91.0	73.3
							252.0	R.S.	78.0	91.0		136.8	128.6			143.2	157.7	100.9	146.0
Mean	158.4	572.8	587.7	164.7	928.7	893.7	171.9	H.T.	75.7	99.0	116.0	117.1	100.8	98.1	98.1	147.4	152.7	107.5	94.7
					,_,,	0,51,	-/	H.W.	63.0	76.7	111.0	96.1	74.3	72.7	72.7	98.2	96.3	106.1	76.9
Std, Dev.	21.4	80.7	113.2	48.3	200.0	162.9	28,2												
								Mean	66.1	80.0	102.0	103.2	90.0	81.2	82.6	125.0	132.9	102.5	93.6
								Std.Dev.	10.9	14.9	17.2	17.9	19.6	15.2	14.8	17.2	20.5	14.0	21.9
ISCHEMIC																			
A.F.	154.3		1050.5	287.3															
R.G.	139.6	893.5	657.3	132.2									ISC	HEMIC					
C.G.	145.9	738.9	03713	208.0															
L.K.	145.5	763.4		172.4				A.F.	85.0	100.0		170.8	148.2						
S.L.	140.4	643.5	653.4	190.5				H.G.	97.1	105.7	108.1	104.9	95.6						
F.N.	160.9	668.6	709.4	171.5				C.G.	66.1	80.7	110.0	79.2	79.0						
C.S.	99.3	670,2	.0,,4	269.2				L.K.	75.0	83.3	114.7	94.2	88.4						
C.S.	130.8	458.5		122.6				J.L.	80.5		114.9	116.7	113.1						
	250.0	430.3		122.0				F.N.	66.6		125.9		89.3						
Mean	139.5	690.9	767.6	194.2				C.S.	68.1		124.3		70.7						
-/		030.9	/0/.0	174.2				c.s.	59.4		104.5		91.6						
Std.Dev.	18.7	132.8	190.3	59.0				Mean	74.7	73.5	114.6	112.0	96.9						

TABLE V

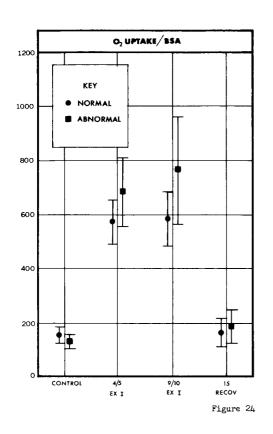
Std.Dev. 12.3 30.8 8.0 47.6 17.3

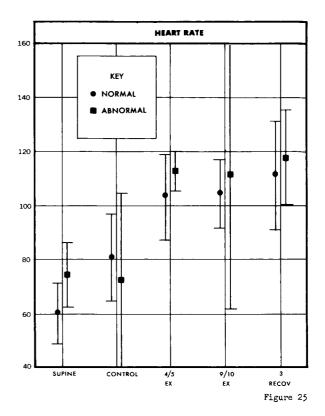
PULSE PRESSURE - HEART RATE PRODUCT								HEART RATE - OXYGEN PRODUCT SLOPE					
			MM Hg/m	in									
			NORMAL				NORMAL.						
	Sup	_ l Std	1 Ex 4/5	1 Ex 9/10	1 Rec 3	1 Rec 15		<u> 8x 1</u>	EXII				
D.A.	3483	3385	6580	8056	4190	5040	_						
в.		6078	10000	10629	7218	4875	В.	.218	. 271				
T.B.	3545	3774	4401	5427	3702	3645	т.в.	.211	.121				
M.D.	2902	3569	7700	6132	4225	3244	T.F.	. 308					
T.F.	4118	4286	5519	1926	5405	3546	W.H.	.200	.103				
W.H.		3200	7163	9248	3528	3668	I.H.	.211					
I.H.		2167	4890	6504	2460	2161	M.L.	.279					
M.L.	4372	2934	6696	6834	4096	2916	C.L.	.126	.073				
E.L.	2668	2392	3526	4257	1764		L.L	227	.088				
C.L.	2324	2280	6916	7648	2492	2504	A.S. R.S.	.337	.096				
L.L.	2944	2029		6420	3562	2124		.219					
A.S.	2208	5530	7920	7700	3066	4000	H.T.	.188	.098				
R.S.	6240	8372	9680	11491	11574		H.W.	.222	.134				
H.T.	4391	3762	4408	10071	2016	4905	w	***					
H.W.	2772	2608	5940	7111	2584	2556	Mean	.229	.123				
Mean	3497	3758	6524	7297	4125	3478	Std. Dev.	.059	.063				
Std. Dev.	1144	1735	1758	2473	2486	1017							
								ISCHEMIC					
			ISCHEMI	С									
							H.G.	.151					
A.F.	4250	2800		13664	5928	2760	C.G.	.145					
H.G.		9224	10042	9729	9966	8604	L.K.	.138					
C.G.	3966	5246	7700		5544	3555	S.L.	.179					
L.K.	3000	2082	6882		3768	3536	F.N.	.145					
S.L.	4025	5664	8618	8752	5655	3640	C.S.	.076					
F.N.	3996	4542	8813	5500	4490	3220	c.s.	.203					
c.s.		5128	9944		5656	5616							
c.s.	2673	2988	3658			3664	Mean	.148					
Mean	3652	4709	7957	9411	5858	4324	Std.Dev.	.039					
Std. Dev.	2044	2246	2204	3363	1971	1918							

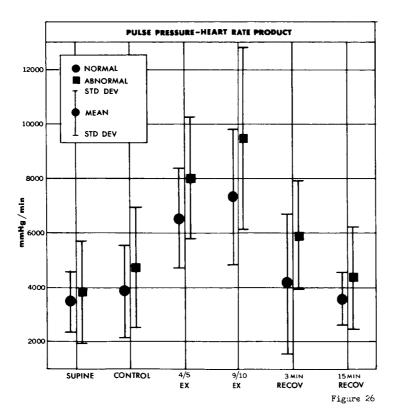
TABLE VIII

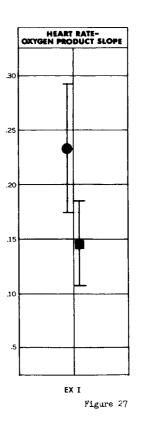
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## 3.32 <u>Heart Rate</u>

The heart rate data from the two groups obtained at the five measurement levels during the test are illustrated in figure 25. As will be noted, the mean values for the normal and ischemic heart rates overlapped by at least one standard deviation at all levels of exercise and recovery.

## 3.33 <u>Pulse Pressure Heart Rate Product</u>

A comparison was made of the product of pulse pressure and heart rate in these two groups in order to determine whether this standard function measurement assisted in discriminating between the two groups. These data are presented in figure 26 which shows that the mean values were practically identical for resting and exercising conditions.

# 3.34 <u>Heart Rate-Oxygen Product Slope</u>

In order to extract all the meaningful information from these data, a combination of parameters which provided the highest level of discrimination between the two groups was formed. This was accomplished by dividing

the product of the resting heart rate oxygen consumption by the product of the four to five minute heart rate oxygen uptake. These data are illustrated in figure 27. The statistical significance of this measurement is of the order of 85%. Although such a measurement has limited usefulness in a study of this type, it is one which has not yet been reported in the literature and may be useful in other studies.

## 3.35 Spectrum Analysis

The purpose of this study was to determine whether differences existed in the precordial vibratory frequency spectra of subjects undergoing exercise. Three subjects were chosen for this study; two were normal and the third had a positive Master 2-step test.

# 3.351 Methods

The exercise consisted of walking on a treadmill at a speed of 1.73 miles per hour on a 10% grade. Records of vibrocardiograms and electrocardiograms were taken at rest, five minutes of exercise, 10 minutes of exercise and after 15 minutes of recovery. These parameters were

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recorded on a Dacord FM tape record. The data obtained from these subjects were subsequently edited to eliminate artifacts and 3 beats from each section transcribed to half-inch tape. Power spectral density analyses were then performed on the vibrocardiographic data by band-pass filtering the signal in 2 cycle band widths from 0 to 100 cps. It was thus possible to display relative amplitude vs frequency. The record was adjusted so that the largest frequency component occupied full scale of the resultant tracing. energy of any section was thus arbitrarily chosen and amplitude comparisons between sections are not possible. In order to obtain comparative data, it was necessary to normalize the frequency-amplitude curves. accomplished by dividing the curve into five cycle band widths and determining the areas under each of the five cycle segments. The areas were then summed, and the percentage of the total energy occupied by each five cycle band width calculated and presented as a function of frequency. A second form of presentation

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was accomplished by summing sequentially the percent energy and presenting the summed values as a function of frequency.

#### 3.352 Results

The summed energy vs frequency curves showed consistent responses in all three subjects. (figure 28) Exercise produced a shift in energy to higher frequencies which returned to control levels in the recovery records.

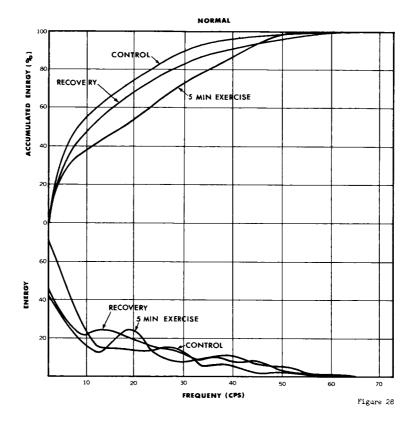
There were no characteristics which differentiated the normal from the abnormal subjects in this method of presentation.

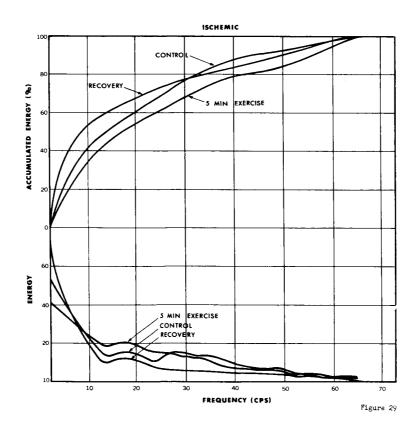
The percent energy vs frequency curves (figure 29) exhibited one major factor which differed between the normal and abnormal subject. In the normal subjects there was an energy peak which shifted during exercise to approximately 10 cps. In the abnormal subject, this energy peak did not shift.

## 3.36 <u>Vibrocardiographic Measurements</u>

The vibrocardiographic ratio (RJ $_2$ /J $_2$ L) was examined

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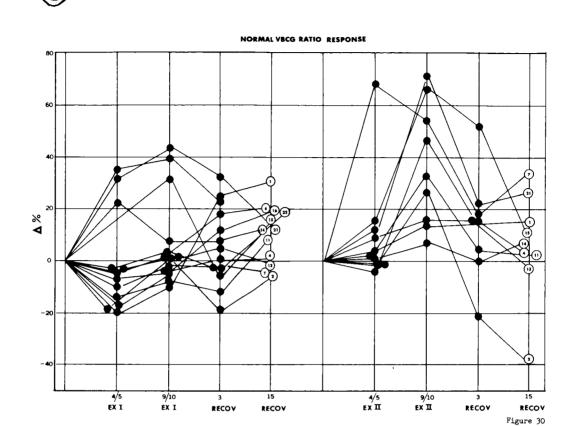


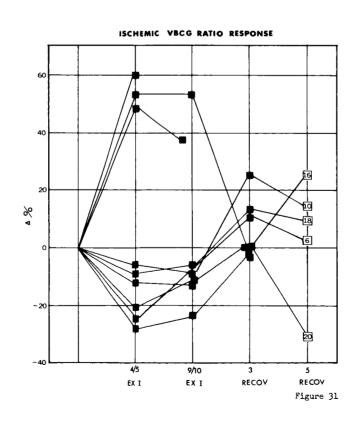


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under resting, exercise and recovery conditions. data are presented in graphic form in Figures 30 and 31. Contrary to the original findings in the Master 2-step studies and the bicycle ergometer studies, the ratio was seen to decrease during the first level of exercise in both the normal and abnormal groups. In the normal group, there was a slight tendency upward of the ratio as the final minutes of exercise were achieved. differences between this group and the abnormal group, however, are not striking and certainly not the same as originally observed in the Master 2-step studies. During exercise level II achieved only in the normal group, a difference in the ratio response was again In the 5th minute of exercise II, the normals generally exhibited an increase of the ratio and during the final minutes of this exercise level, a very large increase in the ratio was noted. The ratio returned to control values after recovery. Thus, if these two exercise studies are combined and the ratio examined as a function of work, there is an initial decrease representing the four to five minute exercise I level

going to no change represented by the nine to ten minute exercise I level, a slight increase represented by the fifth minute of exercise II and a large increase represented by the tenth minute of exercise II. Since the abnormal subjects were not able to complete the second exercise level, a comparison of this type could not be made. In order to verify these findings, the data obtained in these studies were re-examined in several cases. Here, it was possible to read the vibrocardiograms during the one minute interval recordings which were obtained during the test. It was thus possible to calculate the ratio response during minute increments throughout the exercise. These values are presented in figure 32. The uniformity between the normal and ischemic ratio responses is again evident. As a further refinment, the individual intervals of this ratio, the  $R-J_2$  interval and the  $J_2-L$  interval were independently examined and presented in figures 33 and 34. Again, the response is similar between normal and abnormal subjects.





#### ISOMETRIC CONTRACTION PERIOD DURING EXERCISE

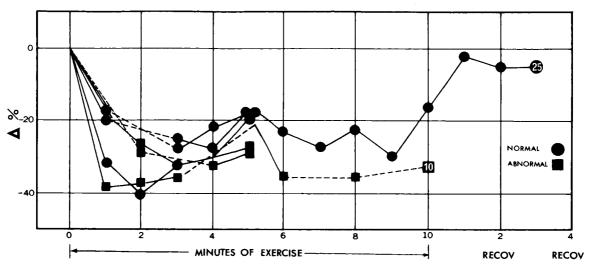
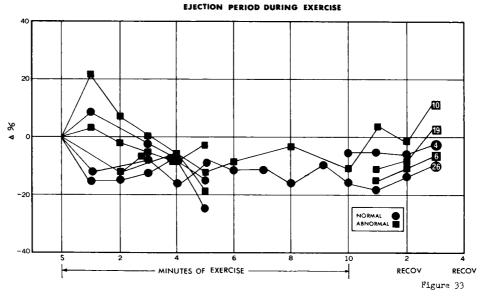
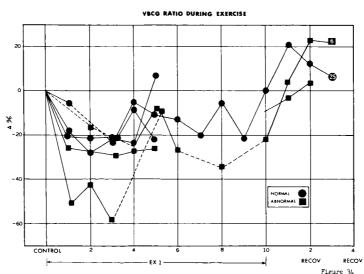


Figure 32





### 3.40 <u>Master 2-step Results</u>

The data obtained in the 2-step studies are presented in tables X, XI and XII. The parameters which were recorded include heart rate and the vibrocardiographic wave intervals. The percentage change of these parameters from resting to exercise conditions is presented in figures 35 and 36. Group IA, the youngest group, illustrated the highest mean ratio change. The subsequent groups IB through IVB save the third group, had nearly the same mean ratio response. Group III which represented the pathologic subjects with cardiac impairment, showed a negative ratio response. comparing the age pared groups, IB and IIIB, the mean values for the percent change of the vibrocardiographic ratio were +12% for the IB group and -14% for the IIIB group. This finding confirms the previous results which were obtained using the vibrocardiographic ratio in response to a 2-step test.

					GROUP I				
Subj.	Age		RJ <sub>2</sub>	J <sub>2</sub> L	HR	$\frac{^{\mathrm{RJ}_2}}{^{\mathrm{J}_2\mathrm{L}}}$	VbCg	ECG	Sub Class
DD	34	c* E R	57 52 61	251 219 246	87 107 93	227 237 248	N	N	A
ST	44		62 53 66	279 197 262	65 91 71	222 269 252	N	N	A
<b>i</b> S	55		51 48 58	297 234 270	72 115 81	179 205 215	N	N	A
rc	41		52 50 5 <b>4</b>	245 194 228	104 115 101	212 258 237	N	N	A
SG	41		35 31 40	308 207 275	64 113 77	114 150 146	N	N	A
SR	45		56 52 58	301 237 279	61 84 71	186 220 208	N	N	A
шм	44		56 50 54	260 210 267	84 102 86	215 238 202	N	N	A
S <b>T</b>	34		46 55 47	278 211 265	87 107 103	165 260 178	N	N	A
rc	45		83 72 -	269 227 -	67 87 -	308 317	N	N	A
SH	35		58 51 51	280 246 285	70 71 71	207 207 179	N	N	A
WB	54		59 59 60	302 215 290	64 93 65	195 274 207	N	N	A
JS	45		58 48 68	314 215 289	65 107 71	185 223 236	N	N	A
HT	53		72 66 70	232 194 220	88 114 93	310 340 318	N	N	A
FÞ	53		45 35 45	303 230 266	63 97 73	148 152 170	N	N	A
PM	38		42 38 44	331 227 322	58 108 65	127 168 137	N	N	A
PS	52		48 51 42	332 220 301	66 110 75	145 232 140	N	N	A
HF	49		62 70 57	284 208 267	66 120 68	218 336 214	N	N	A
EG	67		39 42 55	286 245 260	69 92 65	136 171 212	N	N	В
MP	56		69 60 56	290 237 278	7 <b>4</b> 9 <b>2</b> 87	238 253 202	N	N	В
LM	56		53 41 61	298 212 281	82 104 82	178 193 217	N	N	В
LME	63		61 50 72	259 223 248	92 111 93	236 222 290	A	N	В
мР	62		60 45 59	295 234 287	54 79 64	204 192 206	A	N	В
JR	61		48 40 47	310 249 304	61 82 67	155 160 155	N	N	В
BR	56		55 <b>49</b> 57	315 208 253	54 94 69	175 236 225	N	N	В
wĸ	68		56 45 71	326 245 293	65 94 64	171 184 242	N	N	В
GI	63		48 51	313 253	61 76	153 202	N	N	В

\* C= control, E = exercise, R = recovery

B

GROUP II

				01.001				
Subj.	Age	$RJ_2$	$J_2L$	HIR	RJ <sub>2</sub>	VbCg	ECG	Sub Class
<del></del>					J <sub>2</sub> L			
CM	61 *c	67	300	66	224	N	N	В2
	E	56	222	80	252			
	R	71	280	59	253			
CC	50	51	306	68	167	N	A	Al
		49	234	101	209			
		56	312	69	180			
LRI	56	49	276	70	177	A	A	В
		38	218	103	174			
		49	283	76	173			
LRII	56	47	283	69	166	A	A	В
		36	220	88	164			
		45	205	72	157			
JR	39	68	262	86	<b>2</b> 60	N	N	A2
		62	190	114	326			
		67	272	82	246			
WB	41	63	291	70	216	N	N	Al
		56	212	94	264			
		63	266	72	237			
RA	44	61	316	62	193	N	A	A
		52	257	80	202			
		58	307	66	189			
JG	54	57	317	67	180	N	N	A
		48	214	99	224			
		60	302	77	199			
GG	51	79	315	5 <b>2</b>	250	N	N	A
		55	215	100	256			
		72	295	52	244			
CC	50	50	330	59	151	N	A	Α
		39	232	90	168			
		51	310	55	164			
$_{ m HL}$	53	41	331	60	124	N	N	Α
		40	281	68	137			
		31	338	62	92			

TABLE X

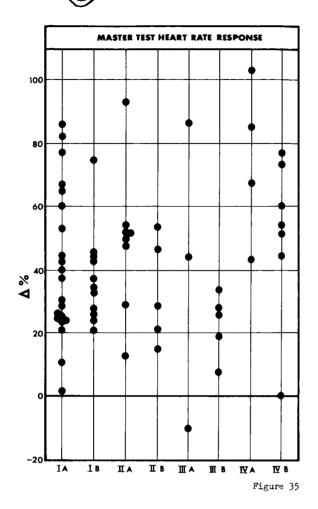
C = control, E = exercise, R = recovery

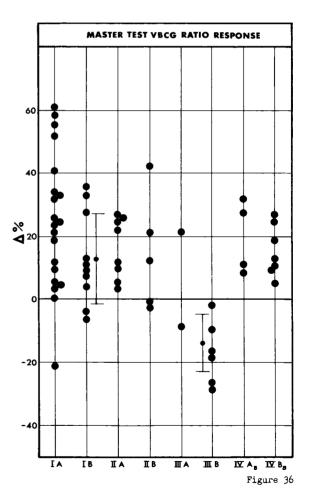
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				GROUP I	II			
Subj.	Age	R-J <sub>2</sub>	J <sub>2</sub> -L	HR	$\frac{^{R-J}_2}{^{J}_2^{-L}}$	VbCg	ECG	Sub Class
ВК	59 °C E R	54 51 54	327 256 334	58 67 56	165 200 162	N	А	В3
PW I	66	<b>41</b> 50 59	297 274 321	69 86 71	206 183 184	A	A	В7
LS	59	60 48 53	263 252 281	83 89 84	228 190 189	Α	A	B7.8
HS	63	61 45 67	282 255 275	79 100 77	216 176 244	A	A	В3
SL	55	57 35 unr	291 246 e a d a	71 102 able	196 142	A	A	A2.3
AR	54	55 50 56	281 205 262	67 124 68	196 243 213	N	Α	A3
PW II	66	54 50 63	284 267 288	73 87 74	190 187 212	А	A	В7
WR	70	70 46 64	288 245 272	62 82 74	243 188 235	A	A	В3
JL	35	48 45 53	280 300 300	87 77 84	171 150 177	А	A	<b>A</b> 3
				GROUP I	v			
Subj.	Age	RJ <sub>2</sub>	J <sub>2</sub> L	HR	$\frac{RJ_2}{J_2L}$	VbCg	ECG	Sub Class
JL	60 C* E R	54 45 58	304 225 296	56 99 61	178 200 196	N	A	B2.7.8
EF	52	52 49 47	276 208 285	75 107 85	188 238 165	N	A	A7.8
NC	56	69 58 63	261 200 268	76 121 92	264 290 235	N	Α	В8
WR	72	62 54 64	279 194 280	69 107 7 <b>4</b>	222 278 220	N	A	в1.8
MD	56	44 40 43	325 251 325	52 90 53	135 160 132	N	A	В8
NL	60	56 45 62	277 211 254	66 99 70	202 213 244	N	A	в7.8
SS	61	61 57 60	307 257 295	56 81 56	199 222 204	N	A	В8
AF	52	80 68 85	243 156 217	83 153 91	330 436 392	N	A	A1.8.
MG	55	50 39 51	282 242 272	57 95 66	179 160 188	А	A	A1.8
TM	58	61 56 65	298 221 310	47 47 42	204 253 210	N	Α	В8
AR	53	62 44 65	340 221 330	61 127 72	182 199 197	none	A	A2.8
			т	ABLE XI				

<sup>\*</sup> C = control, E = exercise, R = recovery





### 3.50 <u>Summary of Exercise Studies</u>

In summary, none of the vital functions including the vibrocardiographic ratio which were recorded during treadmill exercise serve to differentiate between normal and pathologic subjects. However, the vibrocardiographic ratio discriminated at a very high significance level between the normal and pathologic groups using the Master 2-step test. An examination was, therefore, made into the differences between the types of exercise tests which were used in the two series of subjects. The greatest difference between the tests is that the subject is in a constant standing position during treadmill exercise, whereas during the 2-step test, records are taken in a supine position at rest and after exercise while exercise is performed in the standing position. The probable difference, therefore, between the two tests is that the change from the standing to the supine position may impose a stress which is not present in standing exercise, and apparently this postural response is the one which shows differences between normals and pathologics

A re-evaluation was then made of the 2-step data.

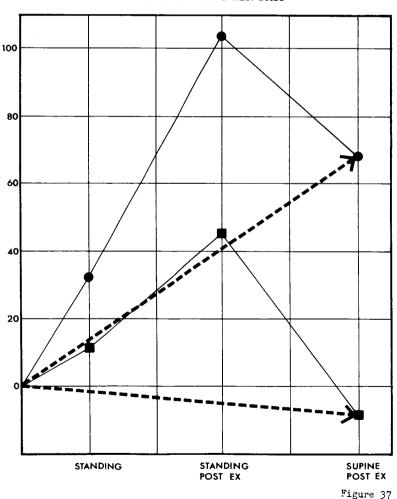
several of these studies, records were taken at so

control, standing control, standing after exercise

several of these studies, records were taken at supine control, standing control, standing after exercise and supine after exercise in order to compare the effects of posture with those of exercise. These experiments are presented in figure 37, and illustrate cases which were previously reported in the section entitled

Master 2-step Tests. As will be noted, there is a

#### MASTER TEST RATIO RESPONSE



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large increase in the ratio from supine control to standing control to standing immediately post-exercise shows an increase in both normal and pathologic subjects. is not until the supine post-exercise state is achieved that differences between normal and abnormals become manifest. It is thus probable that the change in posture from standing to supine induces a stress which is sufficient to differentiate between the two types of subjects. The possible mechanism of this response is that there is an increase in stroke volume from the standing to the supine position which occurs in the absence of contractility The ventricle is suddenly presented with a marked increase in return flow and required to expel a greater stroke volume, and must exhibit an increase in stroke work without changes in its contractile state. This type of stress is probably more severe than that encountered during the exercise state since during exercise changes in contractility are induced by increased sympathetic discharges and increased catecholamine content. If such is the case, the simplicity of a stress test of this type is evident, requiring no exercise or stress

procedures which may be harmful to the subject. These data suggest that tilting or a simple change in position from standing to supine may serve as a valuable function test. This hypothesis is currently being tested.

### 3.60 Human Catheterization Studies

#### 3.61 Methods

The human heart catheterization program has now been initiated utilizing the new transducer-tipped catheter for obtaining intracardiac pressure curves. These studies were under taken to provide a correlation of the vibrocardiogram with left ventricular and aortic pressure phenomena, and to establish the cardiac stress response in the human. For the first phase of the study, the camera-oscilloscope recording technique was used to insure the highest timing accuracy. For the second phase of the study the Electronics-for-Medicine Direct Writer, with a paper speed of 100 mm. per second was utilized. The parameters recorded during these experiments included the vibrocardiogram, electrocardiogram, aortic pressure, left ventricular pressure

derivative and cardiac output (dye method). Angiotensin infusion was used as the stress test.

#### 3.62 Results

Figure 38 illustrates the vibrocardiogram with left ventricular pressure, the first derivative of left ventricular pressure, and electrocardiogram. Figure 39 shows the vibrocardiogram with aortic pressure, the aortic pressure derivative and electrocardiogram. These pressure curves, obtained with the transducer tipped catheter, demonstrate the correlation of the vibrocardiographic H, J<sub>2</sub> and L waves to the onset of ventricular pressure rise, aortic valve opening, and aortic valve closure respectively. The similarity of the vibrocardiogram to the derivative of intraventricular pressure is also apparent.

The data obtained during angiotensin infusion are presented in Table XIII. These measurements consist of left ventricular end-diastolic pressure, systolic and diastolic aortic pressures, the derivative of left ventricular pressure, stroke work, stroke power, systolic resistance, the isometric contraction and ejection periods, and heart rate.

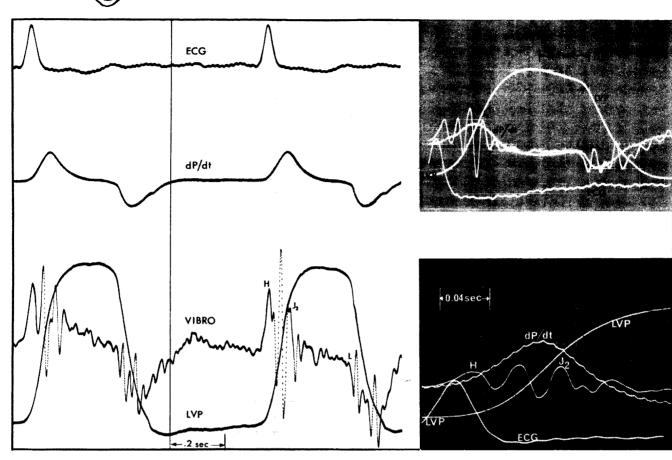


Figure 38

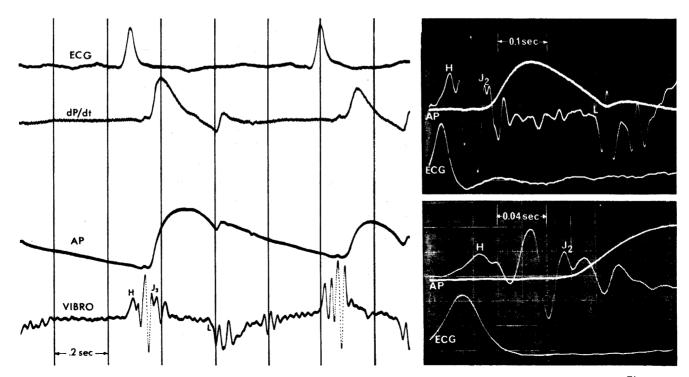


Figure 39

#### HUMAN CATHETERIZATION DATA

	EDP	MSP	<u>sv</u>	MSR	SdP/dt	_SW_	SP	<u>CO</u>	ET	HR
Control	20	138	49	186	1360	67.5	256	2.7	.263	55
ANG 1	28	149			1290				.260	65
ANG 2	36	159			1290				.260	53
ANG 3	34	172			1570					
ANG 4	38	160	49	189	1340	74.0	284	3.5	.260	72

Key: EDP = End Diastolic Pressure (mmHg) = Mean Systolic Pressure (mmHg) MSP

SV = Stroke Volume (ml)

= Mean Systolic Resistance (ml/mmHg) MSR

SdP/dt= Max Systolic dP/dt (mmHg/sec)

SW = Stroke Work (1-mmHg)

SP = Stroke Power (1-mmHg/sec) CO = Cardiac Output (1/min) ET = Ejection Time (secs)

HR = Heart Rate (beats/min) Since only one pilot study of this type has been performed, conclusions cannot be made from these data. However, these parameters will be examined for their applicability in determining cardiac function when a large group of subjects has been studied.

### 3.70 Vibrocardiographic Waveform Analysis

In order to examine more clearly the vibrocardiographic alterations occurring in humans and animals during stress procedures, a more precise means of wave identification was found necessary. A study was undertaken to determine the relationship of all of the systolic and diastolic waves of the vibrocardiogram to the electrocardiographic reference both in resting and stress conditions. objective was to determine whether these intervals were altered merely as a result of heart rate changes per se or whether they changed because of the imposed stress. Human and animal vibrocardiographic data were used in this The human data consisted of supine and standing vibrocardiograms while the animal data consisted of control records obtained from the anesthetized dog and trained intact dogs.

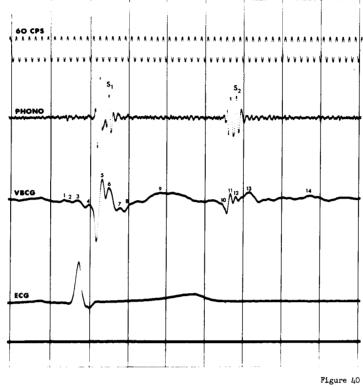
### 3.71 <u>Methods</u>

The waves from representative vibrocardiographic complexes were numbered successively starting with the wave which occurred closest to the Q of the ECG, (figure 40). The distance from the Q-wave to each of these vibrocardiographic waves was then measured and presented as a function of the total cardiac cycle length (R-R interval). In this manner it was possible to establish the distance of each wave point from the electrocardiographic reference and also to examine the variations in these intervals occurring as a function of heart rate as opposed to alterations from other causes.

#### 3.72 Results

The data obtained from this study are presented in figure 41 which shows the alterations of the wave intervals with respect to changes in cardiac cycle length.

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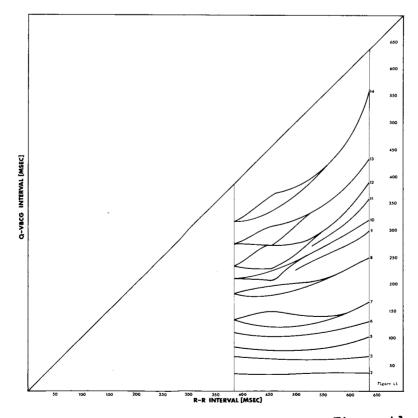


Figure 41

The following cardiac phases are represented by these intervals:

Period	VbCg Interval
Electromechanical lag period	Q - 3
Isometric contraction period	3 - 5
Rapid ejection period	5 - 8
Reduced ejection period	8 - 10
Isometric relaxation period	10 - 13
Rapid filling period	13 - 14
Diastasis and atrial systole	14 - Q

Examination of vibrocardiographic patterns in these subjects has led to more precise criteria for identification of tracings which is based on the morphology of the wave as well as its time from a reference point.

The new criteria for identification of waves are as follows:

- The first VbCg deflection occurs in the ECG P-R interval and is often not clearly discernible.
- 2. The second VbCg deflection occurs with the

- onset of the QRS(ECG) complex.
- 3. This wave occurs with the R peak of the ECG, prior to the onset of the first heart sound and has been previously designated as the H wave.
- 4. This wave coincides with the S wave of the ECG and the onset of the first heart sound. It represents the VbCg  $J_1$  wave.
- 5. The fifth VbCg deflection -- the J<sub>2</sub> wave is generally the highest amplitude deflection in the first sound complex of the VbCg and is marked by the termination of a high frequency wave. It is easily identified by its characteristic morphology.
- 6. This wave occurs with the termination of the first heart sound.
- 7., 8., & 9. These VbCg components occur during the ejection interval and are of low frequency and amplitude.
- 10. This VbCg wave occurs with the onset of the second heart sound and on the descending limb of

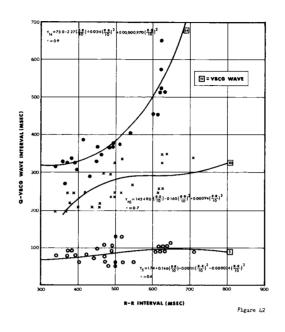
the ECG T wave. It is the first high frequency deflection which marks the termination of systole and has been termed the L wave.

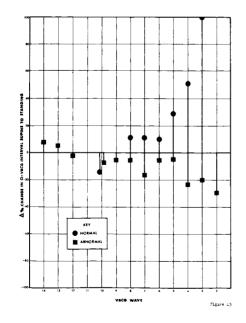
11. - 14. These early diastolic waves occur after the inscription of the ECG T wave and are of low frequency and amplitude.

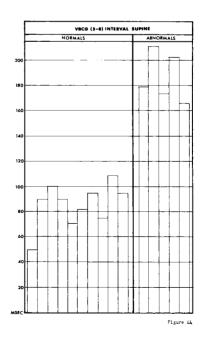
The periods demarked by the VbCg waves are being examined to determine how they are altered by heart rate and stress conditions. This will be accomplished by performing regression analyses on the VbCg interval — heart rate curves for control states. An example of such an analysis is presented in figure 42 where the least squares method was employed to fit curves through the vibrocardiographic 5, 10 and 14 wave. These analyses will establish standard VbCg heart rate curves so that comparisons may be made with data from the stress conditions of hypoxia, hemorrhage, exercise, etc.

The change of the VbCg intervals from the supine to standing position is illustrated in figure 43. Differences

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can be noted between the normal and abnormal, particularly in the 5 - 8 interval, which probably represents the phase of rapid ventricular ejection. In the normal subject, this interval is prolonged upon standing while in the abnormal it is diminished. The duration of the interval in the supine position is also different in the two groups. It is less than 100 MSEC. in the normals while in the abnormals the lowest value achieved was 130 MSEC. and the majority of values were in the region of 150 to 160 MSEC (figure 44). Thus, a means of distinguishing normal from ischemic subjects is presented in the analysis of this time period. Exercise was not required to demonstrate differences.

### Summary and Conclusions

- 1. A means of identifying the vibrocardiographic intervals on the basis of the time elapsed in milliseconds from an electrocardiographic reference and the morphology of the wave forms is presented.
- 2. The variations of these wave forms in normal and abnormal humans and animals as a function

- of the cardiac cycle length is presented.
- 3. A preliminary regression analysis on the variance of these wave intervals with cardiac cycle length is presented.
- 4. The vibrocardiographic interval representing the rapid ejection period was found to discriminate between normal and abnormal subjects under supine conditions. Further, the change in this interval from supine to standing also showed changes which were directionally different in the normal and pathologic groups.
- 5. Typical wave forms were presented for normal, abnormal human and animal subjects, illustrating variations in the vibrocardiographic wave patterns.
- 3.80 <u>Amplitude Calibration of the Vibrocardiogram</u>
- 3.81 <u>Method</u>

Previous investigations on the amplitudes of vibrocardiograms were limited to comparisons

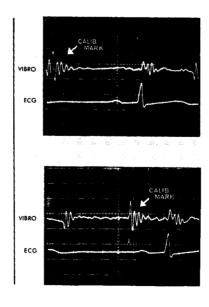
made between individuals because the absolute amplitude of the vibrocardiogram (for a constant electrical amplification) depended on the coupling between the microphone face and the chest (chest-strap tension, thoracic shape, etc.), the position of the heart with respect to the recording site, and the transfer properties of the lung thorax system. A means of amplitude calibration which would compensate for some of these alterations was attempted by dropping a steel ball (6.1 gms.) from 7 cm. height to the chest with the microphone affixed in the standard area. The amplitude of the resultant deflection indicates the resistive properties of the thorax and the degree of microphone coupling. electrical gain of the microphone was adjusted so that a standard deflection was obtained, thus compensating for these properties.

### 3.82 Results

Experiments were performed in three subjects using six positions of the thorax. Figure 45 shows the resultant tracing obtained with the ball dropped in the region

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of the midsternum and second interspace. In this area, the most reproducible curves were obtained. It was also noted that the vibrational wave forms were similar to a damped sine wave, the amplitude of which is given by Y = e<sup>-at</sup> where Y is the amplitude, t is the time of the vibration from onset and a is the resistive constant of the medium. Thus, by examining the log (ln) of the amplitude of the successive vibrations and plotting this as a function of time, a line is obtained whose slope defines the resistive property, a (i.e. lnY= -at). This method provides a means of studying the resistive properties of the thorax as well as a means of amplitude



calibration of the vibrocardiogram.

Figure 45

# 3.90 <u>Human Centrifuge Studies</u>

Pilot experiments were performed at the University of Southern California human centrifuge to determine the feasibility of recording vibrocardiograms from subjects under acceleration loads. The vibrocardiograms were recorded using a Sanborn Recorder with a paper speed of 50 mm/second. Two runs were performed in which the subject was taken to  $2\frac{1}{2}$  G (+Z). In the first run instrumentation difficulties were encountered and it was not possible to record "noise-free" vibrocardiograms. When the appropriate modifications of equipment were made, a second run was attempted and, again, approximately  $2\frac{1}{2}$  G's (+Z) were attained. The records obtained during this procedure are shown in figure 46. As will be noted, the records are readily identifiable and are entirely noise-free. The feasibility of performing such a study utilizing vibrocardiograms with other parameters was clearly established.

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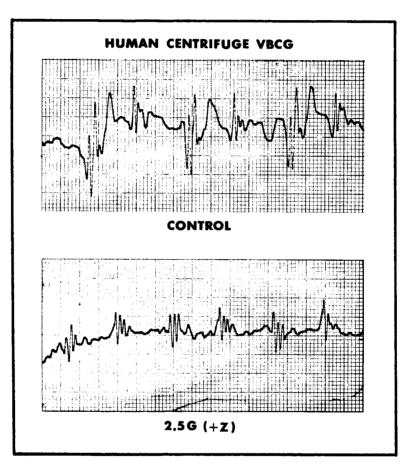


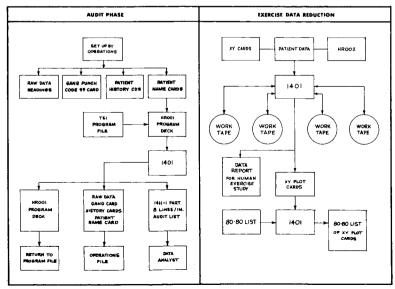
Figure 46

# 4.0 <u>Data Analysis</u>

The facilities of Telecomputing Services Incorporated were utilized for data reduction. Although only limited funds were available for this phase of activity, many useful programs were initiated.

### 4.10 <u>Human Data</u>

In human exercise studies, automatic processing of data included the digitizing of VbCg's, the calculation of intervals, ratios and vital data. This program (indicated in schematic form in figure 47) thus provides accurate computation and facilitates data storage and retrieval. Although this program was developed for exercise testing, it can be used for any type of study.



Purpose

The purpose of chart reading process is to provide accurate linear measurements of certain characteristics of a heart beat of a human patient, as recorded on a vibrocardiogram. The output of the vibrocardiogram is recorded as a continuous function on an oscillogram. The data measurements are of two types:

- A. Sufficient data points to reproduce the characteristics of the wave form.
- B. Measurements of certain indicated events on each heart cycle. Note that one point may be of both types.

A standard exercise is used to stress the heart in order to distinguish between normal and abnormal function. The exercise, generally recorded over 4 cycles, is composed of the following sequence:

- A. Lying Control subject in a supine position.
- B. Standing Control subject standing, prior to exercise.
- C. Exercises 3-4 and 9-10 the subject walks on the treadmill at 1.73 mph on

a 10% grade for 10 minutes. During the 4th to 5th minute and 9th to 10th minute, an air sample is taken, blood pressure measured and an oscillogram made for reduction.

- D. Recovery 3 and 15 minutes this is a recovery period, where the subject sits for the first three minutes and stands for the remaining part of the period. Data is recorded and measured at 3 minutes and 15 minutes.
- E. For the second level of exercise, the treadmill speed is increased to 3.46 mph with the 10% grade. This period is also of 10 minute duration with recordings and measurements being made the same as C above. The recovery cycle is the same as D above.
- F. There is a third exercise level of5.19 mph which may be used in special

cases. This follows the same sequence as the previous exercises and recoveries.

# Chart Identification and Marking

The charts will be annotated prior to submission for reading. The reader should be familiar with this annotation and the significance of the notation (figure 48)

- K This symbol will appear on the ECG trace.

  K identifies the heart beat within the cycle and will generally range from 1 to

  5. Use switch 15 on the Telecordex.
- This symbol will appear above the vibrocardiogram trace. L identifies the test cycle for the patient. Readings over a period of approximately 5 heart beats will be required for each cycle.

  Use switches 7 and 8 on the Telecordex.
- E This symbol will appear above the vibro trace with an arrow extending to a point on the trace. E is a code identification for certain events, J<sub>2</sub>

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being one such event. Use switch 14 on the Telecordex.

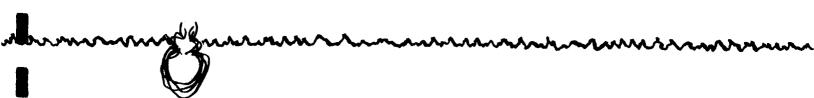
#### Reading Procedure

- A. The record will be read on the Universal Telereader (17A) with a magnification of 2X. Note that the axis convention for X and Y are reversed from normal.
- B. Before starting to read, insert Header

  Card with the information to be duplicated in columns 40 to 80. The names

  on the Header Cards are the same as the

  name on each record. See figure 49.
- C. The record will be read as a time history but the entire record cannot be seen in the field of view on the 17A at one setting of the record. Consequently, when all of the data that can be seen has been read, the record will be advanced. The Time measurement must be accumulative, however. This will be



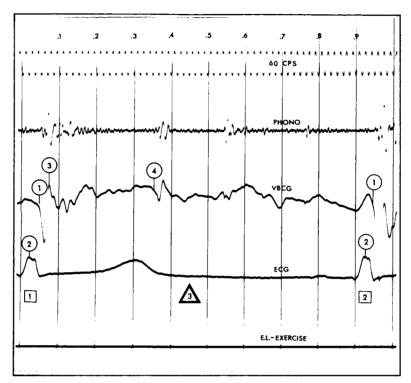


Figure 48

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accomplished by re-zeroing X on the last time point read and entering the accumulated measurement up to this point in the reading cards. (The computer will then be able to compute the accumulated value.)

Interval start time - is the value of the Time, as written on the chart, for the setting of X equal 0. Use switches 1, 2, 3, 4 with the decimal point between switches 2 and 3.

Time of interval - is the delta value of time that will be read before the paper is moved to a new setting. Subtract the time, as marked on the paper, at the X equal 0, to the point of maximum excursion. Use Switches 5 & 6 with the decimal point ahead of Switch 5.

Counts interval - is the value of machine units along the X axis in moving thru the Time interval. Use switches 9, 10, 11 and 12.

D. Mount the record on the machine so that
the first cycle and first heart beat
within the cycle are visible. Check
the direction and assignment of the
accumulators. The beginning of the
record (figure 48) is annotated with
a coordinate system for this purpose.

The arrows indicate the positive X and Y direction. Y = 0 is the point of intersection. The paper should be aligned with the line indicating the X axis.

If the reference line is missing, use the top trace on the record.

E. Set the Telereadex accumulator switches as required. F. Proceed to read the portion of the record that is visible. (There should be at least 20 readings per interval and more if necessary to define the curve. There should be a reading made at each peak, valley and inflection point.) Switch 14 should be set at "Blank" or "Off" for the regular data points and at the Event number, (E), for flagged events. If one point has two flags, read that point twice and flag it in increasing order of event number; i.e., 7 and 3, make one reading with Switch 14 set at 3 and then another reading with the switch set at 7. Then turn the switch to blank and proceed to read the trace.

G. After all of the data in the field of view have been read, advance the record. Set in the constant information and continue reading.

- H. After a new setting is made, the operator should check an output card to verify that the proper data is being punched into the card and that the accumulators are operating properly. This should also be checked periodically throughout the reading process.
- I. After the entire record is read as requested, run out all cards from the machine and label them. Forward the cards and the record to the Supervisor. Any comments regarding problems encountered or abnormalities in the data or equipment should also be brought to the Supervisor's attention.

# 4.20 <u>Animal Data</u>

Programs for the analysis of animal data have recently been completed. These were designed to meet two specific purposes. These were:

1. To correlate VbCg's with all recorded

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hemodynamic parameters.

 To calculate cardiac performance and function measurements under normal and stress conditions.

To achieve these goals, the following means of analysis will be utilized:

Following is the plan for processing the traces from the dog experiments. The purposes of the investigation are:

- To correlate all maxima and minima of the vibrocardiogram with closest hemodynamic event.
- 2. To correlate all labeled hemodynamic events with the closest vibrocardiographic maxima and minima.

These measurements are illustrated in figure 50 and are described below.

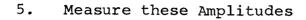
- 3. Provide measurement of the duration of the following events:
  - a. 1-2 isometric contraction
  - b. 2-3 rapid ejection
  - c. 3-4 reduced ejection

- d. 4-5 proto diastole
- e. 5-6 isometric relaxation
- f. 6-1 diastasis + atrial systole

  The start of each of these six events are indicated on

  the traces by numbers 1 through 6. The times between

  successive vertical time lines on all traces is 0.1 second.
  - 4. Measure the following areas:
    - A. Above line through points x & y on flow trace (#2) and between adjacent verticals through 1 where x & y are a pair of points on the flow trace indicating zero flow.
    - B. Pressure baseline (PB) under left ventricular pressure trace (#5) and ventricals
      through 1 and 2.
    - C. Above line parallel to PB through 2 on LVP curve (#5), below aortic pressure curve (#4) and between vertical through 2 and 5.
    - D. Between verticals 2 and 5 above PB and below C.
    - E. Above PB under #5 between verticals through 5 & 6.



- I. PB to intersection of 2 with curve #5.
- II. PB to horizontal through peak LVP, #4.
- III. PB to horizontal through 1 on #5.
- IV. Line through two successive W's and
   maximum LV, #2, where W is a point on
  #3 indicates zero change in LVP, #4.
- V. Line through two successive W's minimum LV, #3.
- VI. Horizontal through x & y and maximum flow, #2.

For all amplitude measurements, a calibration factor is indicated on each chart for each condition and all y-values must be multiplied by that factor.

#### 6. Calculations

- a. Stroke Volume Area A
- b. Stroke Work Area AxArea C ÷ period 2 5
- c. Stroke Power

  Area AxArea C

  (period 2 to 5)<sup>2</sup>
- d. Stroke Volume (SV) =  $\underbrace{\text{A.F. x C.F. x period 1 to 1}}_{60}$

ngg...

e. Stroke Work (SW) = 
$$\underbrace{SV \times area C}_{period 2 to 5}$$

f. Stroke Power (SP) = 
$$\frac{SW}{\text{period 2 to 5}}$$

\*A.F. = Area factor obtained by dye dilution curve which will be supplied with each condition.

\*\*C.F. = Calibration factor - supplied with each trace.

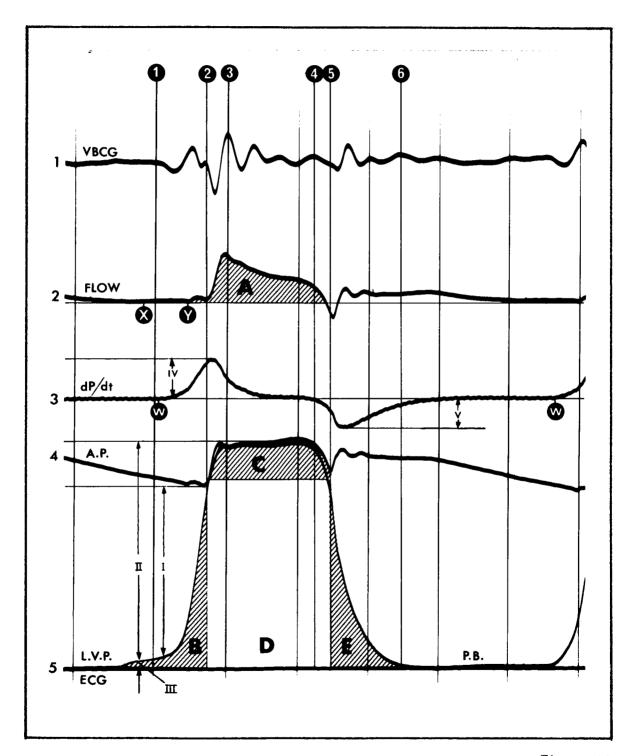


Figure 50

# 5.0 <u>Publications</u>

The documents which have been published during the initial phase of the current grant are listed below. Papers which are currently in preparation and will be published prior to the termination of the grant are also listed.

### 5.10 Published Articles

- 1. Agress, C.M., Nakakura, S.; Variations of the Vibrocardiogram Over the Precordium; Aerospace Medicine; vol. 35, no.8, Aug. '64.
- 2. Agress, C.M., Wegner, S., Nakakura, S.; Measurement of Cardiac Events by a Precise Technique; Comparison with Vibrocardiogram; Jap. Heart J.; Sept. '64, Vol. 5, No. 5, p. 414.
- 3. Nakakura, S., Wegner, S., Agress, C.M.; Influence of Heart Rate on the Phases of the Left Heart Cycle in exercise; Jap. Heart J.; (to be published).

# 5.20 <u>Articles in Preparation</u>

- The Ejection Time Heart Rate Relationships in Normal and Ischemic Subjects. Agress, C.M., Wegner, S., Nakakura, S., Lehman, E., Jr., Chait, L. J. Applied Physiol.
- The Comparison of Posture Changes and Exercise in Normal and Ischemic Subjects Agress, C.M., Wegner, S., Nakakura, S. Geller, P.J. Circ. Research.

- 4. Ventricular Volume Measurements of Treadmill-Trained Dogs Agress, C.M., Wegner, S.
- 5. Use of Vibrocardiogram to Measure Ventricular Volume changes in Animals
- 6. Effects of Experimental Acute Infarction on Ventricular Function Measurements
- 7. The Electropressor Latency Interval in Normal and Ischemic Dogs as Function Measurement.
- 8. Spectrum Analysis of Vibrocardiogram.
- 9. Use of the Vibrocardiogram as a Monitor of Hemodynamic Events.